

**Rx FOR GENERIC DRUG SAFETY: ACCURATE
INFORMATION FOR OLDER AMERICANS**

HEARING

BEFORE THE

**SUBCOMMITTEE ON HOUSING AND CONSUMER
INTERESTS**

OF THE

**SELECT COMMITTEE ON AGING
HOUSE OF REPRESENTATIVES**

ONE HUNDRED FIRST CONGRESS

SECOND SESSION

MARCH 1, 1990

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Rx FOR GENERIC DRUG SAFETY: ACCURATE INFORMATION FOR OLDER AMERICANS

THURSDAY, MARCH 1, 1990

**U.S. HOUSE OF REPRESENTATIVES,
SELECT COMMITTEE ON AGING,
SUBCOMMITTEE ON HOUSING AND CONSUMER INTERESTS,
Washington, DC.**

The Subcommittee met, pursuant to notice at 9:37 a.m., in room 2220, Rayburn House Office Building, Hon. Marilyn Lloyd (Chairman of the Subcommittee) presiding.

Members present: Representatives Lloyd, Bilbray, Pallone, and James.

Staff present: Brian Lindberg, Staff Director; David Dean, Professional Staff; and Mary Graham, Professional Staff.

OPENING STATEMENT OF CHAIRMAN MARILYN LLOYD

Ms. LLOYD. The Subcommittee will come to order. Good morning, ladies and gentlemen. I'm certainly pleased to be here this morning to convene this hearing of the Subcommittee on Housing and Consumer Interests. The purpose of this morning's hearing—my first since becoming Chairman of the Subcommittee—is to review recent serious developments in the generic prescription drug industry, and generate recommendations for older Americans who rely on generic drug products.

Specifically, we will learn what it is like to be an older consumer of generic drugs in a climate of media-hyped findings of fraud in the industry and Government. We will hear from the generic drug industry and the FDA to learn more about how far they have come in policing themselves and protecting consumers. And health professionals and advocates will report to us on how older adults can be wiser consumers of prescription drugs.

In the past several months, serious breaches of integrity in the generic industry have occurred. The discovery of fraudulent acts by officials in both the generic drug industry and the Food and Drug Administration have seriously undermined the confidence of some physicians, pharmacists, and consumers in generic drugs as safe and effective alternatives to more expensive brand-name products. In addition, these developments have rekindled old arguments that generic products are inferior. Frankly, older Americans are afraid to take their medications, and this poses critical health care risks.

I would like to commend my colleague in the House, the Chairman of the Committee on Energy and Commerce, the Honorable John Dingell, for bringing this scandal into public view through a

dramatic series of hearings last year. Only by fully exposing these individuals who have compromised the integrity of the industry can we ultimately fully restore the confidence of consumers of all ages.

The underlying issue of course is the skyrocketing cost of health care for all Americans. This "black hole" attracts and consumes more and more money every day, every month, and every year. Although Medicare is helping to cover the health care costs for most older Americans, beneficiaries are asked to bear a large and increasing portion of the cost of medical services as a result of copayments, deductibles, premiums, and other costs not covered by Medicare. In addition, Medicare does not cover the cost of most prescription drugs that older persons need to maintain their health.

In fact, for three out of four older Americans, the cost of prescription drugs is their largest out-of-pocket health care expense. Only the cost of long-term care for the elderly exceeds the amount that's spent on prescription drugs. Although older adults represent just 12 percent of the Nation's population, they purchase approximately 30 percent of prescription drugs due to their higher incidence of chronic and acute conditions.

Furthermore, over 15 percent of the elderly who use prescription drugs report they are unable to pay for their medications. In my home State of Tennessee, the situation for older adults is especially bleak because 25 percent of the population over age 65 live in poverty.

This situation is getting worse. The provisions of the Medicare Catastrophic Coverage Act that would have covered the cost of outpatient prescription drugs after a deductible were repealed, and the cost of prescription drugs is rising much faster than inflation. From 1981 to 1988, prescription drugs increased in cost by 88 percent while the Consumer Price Index increased only 28 percent.

Until recently, generic drugs were a bright spot in the fight to control spiralling drug costs. Generics, which are generally accepted to be therapeutically equivalent to the brand-name drugs, cost an average of 30 to 50 percent less than the brand-name alternatives. For many low-income older Americans, generics mean the difference between affording necessary medications and going without.

Since the passage of legislation to remove the barriers to generic competition in 1984, the number of applications to the Food and Drug Administration to market generic copies of brand-name drugs has greatly exceeded the agency's ability to review and then approve all of them.

The flood of applications to market new generic drugs coincided with severe budget and staff cuts that occurred during the Reagan administration. Staff levels were reduced from a high of approximately 8,000 to below 7,000. In addition to being unable to process the backlog of new generic drug applications, lacking the proper staffing, the FDA has been unable to vigorously pursue enforcement and issue citations to manufacturers who do not meet industry standards. It was in this climate that a serious regulatory failure occurred. I think that you can look at the staffing levels on the first chart, on chart 1.

FDA staff levels, excluding those working on AIDS-related projects, declined from 7,816 in 1980 to 6,829 in 1989, a reduction of 12.9 percent. Incredibly, these staff reductions came at a time of increased legislative responsibilities, dramatic health care crises such as AIDS, and record numbers of new drug applications. It seems that we're asking the FDA to perform an impossible task: continue to provide the quality safeguards for consumers while Congress continues to reduce staff levels.

Then, of course, as you look at the applications on chart 2, the FDA has been unable to really keep pace with the incredible volume of new drug applications since 1984. Of course, for every year that FDA does not keep pace with the number of drug applications received, the level of pending new applications increases.

The information in both these charts gives us cause for alarm. The delay in processing drug applications harms consumers of prescription drugs by hindering access to the new products.

I very much look forward to the testimony of our witnesses and know that their participation will be thought-provoking and will provide the committee and the Congress with important and meaningful insights and recommendations.

[The prepared statement and supplemental material submitted by Ms. Lloyd follows:]

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 SUBCOMMITTEE ON HOUSING AND CONSUMER INTERESTS

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**RE FOR GENERIC DRUG SAFETY:
 ACCURATE INFORMATION FOR OLDER AMERICANS**

A Hearing of the
 Subcommittee on Housing and Consumer Interests
 Select Committee on Aging
 United States House of Representatives

Opening Statement
 The Honorable Marilyn Lloyd
 Chairman

Thursday, March 1, 1990
 9:30 - 11:30 a.m.
 2220 Rayburn House Office Building

Good Morning. I am pleased to be here to convene this hearing of the Subcommittee on Housing and Consumer Interests. The purpose of this morning's hearing -- my first since becoming Chairman -- is to review recent serious developments in the generic prescription drug industry, and generate recommendations for older Americans who rely on generic drug products.

Before I describe the issue in more detail, I would like to say that I am extremely pleased to chair the Aging Committee's Housing and Consumer Interests Subcommittee. I believe the subcommittee can play an important role in Congress advocating for greatly needed housing and consumer protections for older adults. The matter before us today is an appropriate beginning for that advocacy.

Specifically, we will learn what it is like to be an older consumer of generic drugs in a climate of media-hyped findings of fraud in the industry and government. We will hear from the generic drug industry and the FDA to learn more about how far they have come in policing themselves and protecting consumers. And health professionals and advocates will report to us on how older adults can be wiser consumers of prescription drugs.

Hon. Marilyn Lloyd
March 1, 1990
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In the past several months, serious breaches of integrity in the generic industry have occurred. The discovery of fraudulent acts by officials in both the generic drug industry and the Food and Drug Administration have seriously undermined the confidence of some physicians, pharmacists, and consumers in generic drugs as safe and effective alternatives to more expensive brand name products. In addition, these developments have rekindled old arguments that generic products are inferior. Frankly, older Americans are afraid to take their medications, and this poses critical health care risks.

I would like to commend my colleague in the House, the Honorable Chairman of the Committee on Energy and Commerce, John Dingell, for bringing this scandal into public view through a dramatic series of hearings last year. Only by fully exposing those individuals who have compromised the integrity of this industry can we ultimately fully restore the confidence of consumers of all ages.

The underlying issue, of course, is the skyrocketing cost of health care for all Americans. This "black hole" attracts and consumes more and more money every day, every month, and every year. Although Medicare is helping to cover the health care costs for most older Americans, beneficiaries are asked to bear a large and increasing portion of the cost of medical services as a result of copayments, deductibles, premiums, and other costs not covered by Medicare. In addition, Medicare does not cover the cost of most prescription drugs that older persons need to maintain their health.

In fact, for three out of four older Americans, the cost of prescription drugs is their largest out-of-pocket health care expense. Only the total cost of long-term care for the elderly exceeds the amount spent on prescription drugs. Although older adults represent just 12 percent of the Nation's population, they purchase approximately 30 percent of prescription drugs due to their higher incidence of chronic and acute conditions.

Furthermore, over 15 percent of the elderly who use prescription drugs report they are unable to pay for their medications. In my home State of Tennessee, the situation for older adults is especially bleak because 25 percent of the population over age 65 live in poverty.

Hon. Marilyn Lloyd
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This situation is getting worse. The provisions of the Medicare Catastrophic Coverage Act that would have covered the cost of outpatient prescription drugs after a deductible were repealed, and the cost of prescription drugs is rising much faster than inflation. From 1981 to 1988, prescription drugs increased in cost by 88 percent while the Consumer Price Index increased only 28 percent.

Until recently, generic drugs were a bright spot in the fight to control spiralling drug costs. Generics, which are generally accepted to be therapeutically equivalent to brand name drugs, cost an average of 30 to 50 percent less than brand name alternatives. For many low-income older Americans, generics mean the difference between affording necessary medication and going without.

In order to increase competition in the generic drug market and increase the availability of lower cost generic drugs, we in Congress passed the "Drug Price Competition and Patent Term Restoration Act," in 1984. This law removed barriers to generic competition, and set up a formula to provide money for researching new drugs. Since 1984, the number of applications to the Food and Drug Administration to market generic copies of brand name drugs has greatly exceeded the agency's ability to review and approve all of them.

The flood of applications to market new generic drugs coincided with severe budget and staff cuts that occurred during the Reagan administration. Staff levels were reduced from a high of approximately 8,000 to below 7,000. In addition to being unable to process the backlog of new generic drug applications, lacking proper staffing, the FDA has been unable to vigorously pursue enforcement and issue citations to manufacturers not meeting industry standards. It was in this climate that a serious regulatory failure occurred.

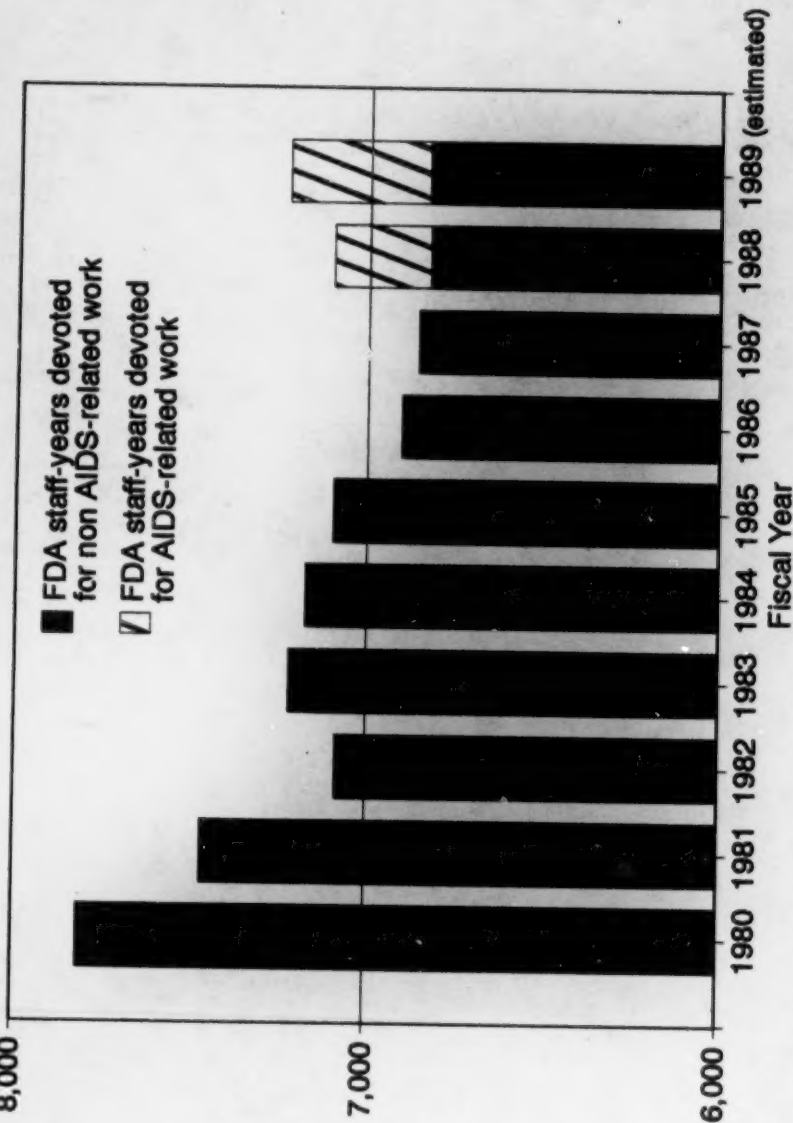
I am pleased to say we have an exemplary line up of witnesses who will discuss the thorny issue of fraud in the generic prescription drug industry. We are fortunate to have a older consumer of prescription drugs here to describe her experiences and two advocates to discuss their work to assist older consumers in getting the most for their drug purchasing dollar. We will also hear recommendations for older consumers on how to evaluate the

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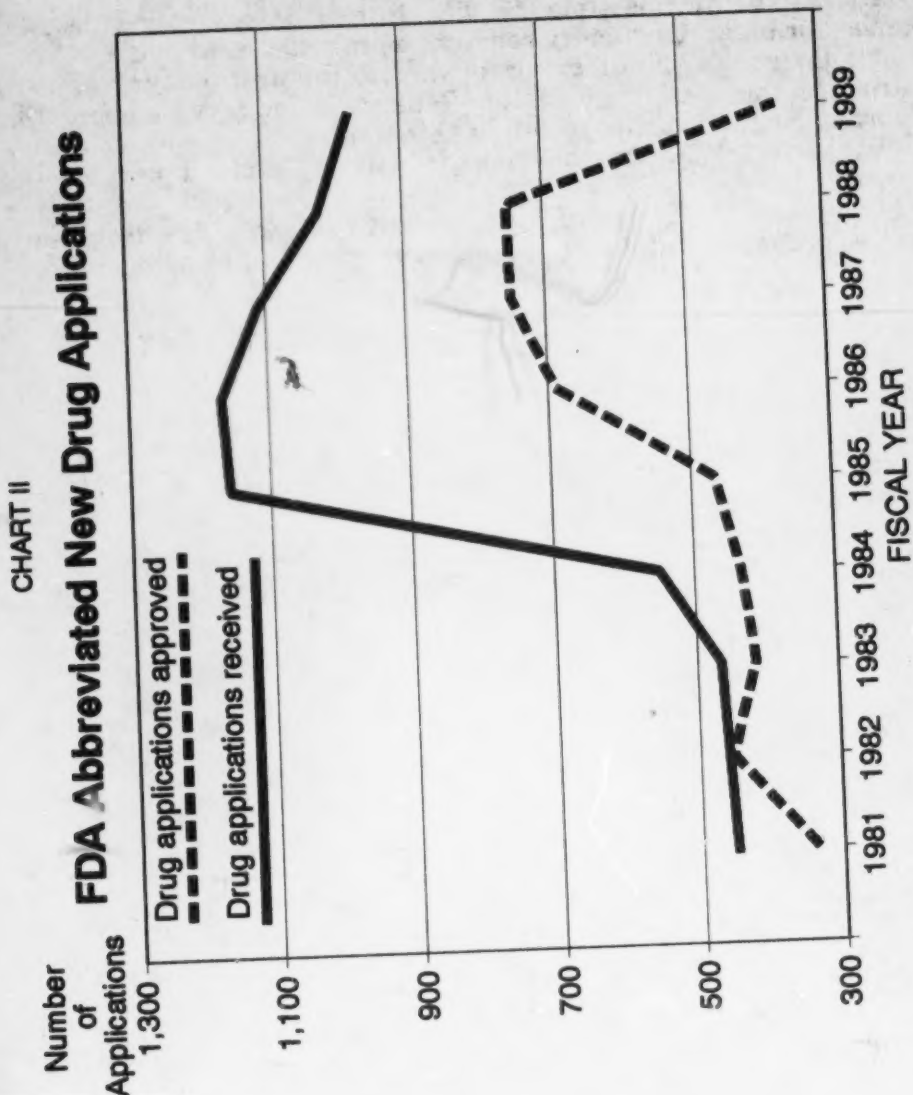
costs, benefits, and risks involved in future drug purchasing decisions. Finally, I am anxious to hear an update from the FDA regarding reforms in the regulatory process that have occurred as a result of last summer's report from the Office of the Inspector General.

I very much look forward to the testimony of our witnesses and know that their participation will be thought-provoking and will provide the committee and the Congress with important and meaningful insights and recommendations.

CHART I
Food and Drug Administration (FDA) Staffing Levels
 Staffing Level



Source: United States General Accounting Office; Report on FDA Resources (GAO/HRD-89-142), September, 1989.



Source: Food and Drug Administration, 1990.

Ms. LLOYD. At this time, I'd like to call on my colleague, Mr. James, for any introductory remarks he might like to make.

Mr. JAMES. Yes. I'm looking forward to this testimony. I want to introduce the statement of the Ranking Minority Member, Jim Courter, for the hearing record at this time.

Ms. LLOYD. Without objection, it will be made a part of the record.

Mr. JAMES. Thank you. I look forward to hearing the testimony.
[The prepared statement of Representative Jim Courter follows:]

PREPARED STATEMENT OF REPRESENTATIVE JIM COURTER

Madam Chairwoman, I am very pleased that the Subcommittee is considering this morning the critical issue of the safety of our nation's supply of generic drugs.

Countless older Americans, particularly those living on fixed incomes, rely on generic drugs to ease the heavy financial burden of medical care. For some seniors, the availability of generic drugs determines whether they can meet their health care costs without foregoing other basic necessities.

However, in recent months many seniors have found that when they go to their medicine cabinets, they have to question whether it is more dangerous to take their generic drugs or forgo their medication.

Recent reports of improprieties and outright fraud during the FDA's generic drug approval process have left individuals throughout the country confused and concerned about the safety and effectiveness of the generic medications they take. Consumers are understandably upset to learn that several FDA reviewers have pleaded guilty to accepting bribes from generic-drug companies. They are worried when they hear that scores of medications have been recalled because of improprieties in the manufacturer's applications to the FDA.

The public has been receiving conflicting information about the safety of our nation's generic drug supply. Outgoing FDA

Commissioner Frank Young stated in Congressional testimony late last year that the FDA had seen "no evidence to date indicating that generic medications now in use pose a serious safety threat." Yet in the same testimony, Commissioner Young informed Congress that "findings from our inspections of generic-drug firms indicate a disturbing level of violations."

Considering these discrepancies, what are senior citizens and consumers in general supposed to believe about the safety of generic drugs? Obviously, the accuracy and reliability of the information upon which FDA approval is based has been called into question.

What we all need now is accurate information. If generics are not safe and effective, senior citizens and their physicians must know so they can make alternate arrangements. If generics are safe and effective, then we must get that message out so that senior citizens can take advantage of the cost savings without risk.

It is my hope that the FDA will be able to provide us with a clearer picture this morning of exactly what consumers should know about generic drugs. I am also hopeful that the agency will follow through on its commitment to providing legislative recommendations for Congress to improve the ability of the FDA to combat abuses in the generic drug approval process.

We must restore the faith of the public in our nation's generic drug supply. We cannot allow seniors to forgo needed medicine because of fear and confusion. It is my hope that today's hearing will shed new light on this critical matter.

Ms. LLOYD. Do you have a statement that you'd like to make at this time?

Mr. JAMES. No, no statement at this time, thank you. I'd like permission to submit one later for the record.

Ms. LLOYD. Without objection, it will be made a part of the record.

[The prepared statement of Representative James follows:]

STATEMENT OF REPRESENTATIVE CRAIG T. JAMES

On behalf of my constituency, I would like to take this opportunity to express my concerns over the results of recent probes of the generic-drug industry. The fraudulent actions of those individuals involved are deplorable. Unfortunately, I believe that their breach of public trust will have severe ramifications which last long into the future. I am especially concerned over the impact it already has shown on this nation's elderly population.

According to the American Association of Retired Persons, Senior Citizens spend more on prescriptions than for any other health-related need except for long-term care. With generic-drugs typically offering a savings of 50% over their brandname counterparts, such alternatives offer an economically advantageous option to those living on fixed incomes. However, the recent controversy surrounding the generic industry have cast doubt in the minds of our elderly. Not only do they feel betrayed by the pharmaceutical industry, but they believe they were sold out by their own government.

As a representative from Florida, my constituency includes a great number of older Americans. In fact, nearly one-fifth of my district is currently 65+ years of age. For these people, I fear that it will take more than a hearing on this subject to rebuild their faith. We, as members of Congress, pharmaceutical companies, drug regulatory agencies, must do all we can to reinstate the elderly's confidence in their medications. I look forward to the forthcoming testimony on recent actions and the recommendations for future efforts.

Ms. LLOYD. At this time I would like to submit the prepared statement of Mr. Bilbray for the hearing record. Hearing no objections, so ordered.

[The prepared statement of Representative Bilbray follows:]

PREPARED STATEMENT OF
REPRESENTATIVE JAMES H. BILBRAY

MADAME CHAIRWOMAN, I'D LIKE TO START BY CONGRATULATING YOU ON ATTAINING THE CHAIRMANSHIP OF THIS IMPORTANT SUBCOMMITTEE. AS MEMBERS OF THIS SUBCOMMITTEE, WE ARE IN A POSITION TO EXAMINE AND INVESTIGATE A WIDE RANGE OF ISSUES THAT ARE OF GREAT IMPORTANCE TO OUR NATION'S ELDERLY, AND I LOOK FORWARD TO WORKING TOGETHER WITH YOU AND THE OTHER MEMBERS OF THE SUBCOMMITTEE ON WHAT I HOPE WILL BE A VERY PRODUCTIVE SERIES OF HEARINGS THIS YEAR.

MADAME CHAIRWOMAN, ENSURING THE SAFETY OF OUR NATION'S DRUG SUPPLY MOST CERTAINLY IMPACTS ALL

AMERICANS, BUT IT HAS A SPECIAL EFFECT ON OUR NATION'S SENIOR CITIZENS. SENIORS ARE DEPENDENT UPON GENERIC DRUGS FOR A VARIETY OF REASONS, INCLUDING THEIR LOW COST RELATIVE TO BRAND NAME PHARMECUETICALS, AND THEIR WIDE SPREAD AVAILABILITY THROUGH MAIL ORDER PHARMACIES.

THE ALLEGATIONS THAT SURFACED DURING LAST YEAR'S GENERIC DRUG SCANDAL ARE WELL KNOWN. NOW THAT WE WILL HAVE A NEW FDA DIRECTOR, AND WHAT I HOPE WILL BE A NEW FDA MANAGEMENT TEAM, WE MUST LOOK TOWARD THE FUTURE, AND ASK WHAT CONTROLS HAVE BEEN PUT INTO PLACE

TO ENSURE THAT SUCH A SCANDAL DOES NOT OCCUR AGAIN.

GENERIC DRUGS ARE FAR TOO IMPORTANT TO OUR SENIORS TO EVER LET A SIMILAR SCANDAL OCCUR. FOR MANY SENIOR CITIZENS, THE GENERIC DRUGS THAT THEY CONSUME ARE NOT UNNEEDED LUXURIES; RATHER, IN MANY INSTANCES, THEY CAN BE THE DIFFERENCE BETWEEN LIFE AND DEATH. WITH HEALTH CARE COSTS CONTINUING TO RISE AT DOUBLE DIGIT RATES EVERY YEAR, GENERIC DRUGS WOULD SEEM TO BE AN INVALUABLE PART OF ANY OVERALL PLAN TO BRING THESE COSTS UNDER CONTROL. HOWEVER, IF WE CANNOT ASSURE THE SAFETY OF THE

GENERIC DRUG SUPPLY TO THE AMERICAN PUBLIC, THEN WE WILL MOST CERTAINLY LOSE THIS OPTION.

WE HAVE A DISTINGUISHED PANEL HERE TODAY THAT REPRESENTS THOSE ON ALL SIDES OF THIS ISSUE. I LOOK FORWARD TO THEIR TESTIMONY, AND TO LEARNING WHAT SPECIFIC MEASURES ARE BEING TAKEN TO PREVENT A REPEAT OF LAST YEAR.

Ms. LLOYD. We're looking forward to our first witnesses here. We have Ms. Geraldine Brooks, who is from Washington, DC. We have Ms. Kathleen Col with us and Ms. Cheryl Fish-Parcham.

We welcome all three of you.

Ms. Col, I believe you are our lead witness. Please proceed.

STATEMENT OF KATHLEEN COL, CONGRESSIONAL DISTRICT COORDINATOR, AMERICAN ASSOCIATION OF RETIRED PERSONS VOTE PROGRAM, MIAMI, FLORIDA

Ms. COL. Good morning, Madam Chairman. My name is Kathleen Col, and I'm a congressional district coordinator for the AARP VOTE program in Florida.

On behalf of the AARP, I'm pleased to be able to discuss with this Subcommittee the problem that paying for prescription medications presents and the important role that generic drugs play in making medications affordable. While AARP strongly believes in improving consumer awareness about costs, benefits, and potential risks associated with prescription medications, we also believe that the ultimate responsibility for determining whether generic drugs are safe and effective must be borne by the FDA.

Older Americans consume a disproportionately large share of prescription drugs. Persons aged 65 and older represent only 12 percent of the American population, yet they consume 30 percent of the prescription drugs.

In 1987, the mean expenditure for prescribed medication for non-institutionalized elderly was up 110 percent from 1980—110 percent. Between 1980 and 1989, prescription drug prices rose by 128 percent compared with an increase in the general inflation rate of just over 50 percent. In 1989 alone, when the overall rate of inflation was 4.8 percent, average prescription drug prices rose by 8.7 percent.

High prices, heavy utilization, and the absence of affordable coverage in the private "medigap" marketplace have converged to make prescription drugs the second highest out-of-pocket medical expense for older people. These high prices also affect the behavior of older Americans. According to a report by the Public Health Service, 15.5 percent of elderly patients who require prescriptions said that they are unable to pay for their drugs.

Anecdotal accounts of older persons modifying their prescription drug regimens because of financial constraints are numerous. Drugs are among the most cost-effective of medical care components.

Noncompliance with prescribed drug regimens may result in more costly physician visits or even hospitalization. It may also contribute to the already serious problem of mismedication among older Americans.

Recent improprieties uncovered within the Food and Drug Administration and the generic drug industry have given rise to serious concerns about the integrity of the approval process for generic drugs. While it remains true that there has not been a documented report of an injury involving the use of any of these bioequivalent generic drugs approved since 1970, public confidence has been threatened.

In 1989 about one-fourth of prescriptions for noninstitutionalized Medicare beneficiaries were filled with generic drugs. In general, the cost of generics is about 30 to 50 percent of their brand-name counterparts. If confidence in these drugs declines, then people may be less willing to replace expensive brand-name drugs with their more cost-effective generic counterparts.

The public must have confidence that all drugs, brand-name and generic, meet the same rigorous FDA standards for purity, strength, and quality. AARP has always urged patients to consult their physician with any questions about their medications, including the decision whether to use a generic drug. This advice becomes even more important now.

AARP provides a number of sources of assistance on prescription drugs. In 1989, for example, the association conducted a drug price survey of more than 1,000 pharmacies in 42 States. The results of the survey were published in August along with two new free AARP publications: "The Smart Consumer's Guide to Prescription Drugs" and the "Consumer Pharmacy Surveys: A How-To Kit."

Additionally, AARP's monthly news publication, the AARP Bulletin, regularly addresses issues relating to prescription drugs. For example, recent articles have focused extensively on the generic drug industry.

Further, AARP's pharmacy service assists older people in the safe and efficient use of prescription drugs, such as individual patient profiles, sophisticated computer software on drug interaction, and a toll-free telephone service to patients to assure easy access to a pharmacist when any questions arise.

One of the pharmacy service's most important initiatives is to provide specially-designed informational leaflets for specific drugs. They inform the patient what the drug is, what it is used for, how to take it, what side effects to be aware of, and what questions to ask the prescriber. These pamphlets are developed with the assistance and cooperation of the Food and Drug Administration and other experts. They cover over 500 drugs.

In conclusion, Madam Chairman, let me note again that recent revelations of improper practices by several generic drug firms, as well as some FDA staff, threaten public confidence in generic drugs. AARP is committed to improving consumer information about prescription medications, including generic drugs. AARP believes that the responsibility to ensure the safety and efficacy of generic drugs must be with the FDA.

We look forward to continuing to work with members of this committee and the Congress to ensure that consumer information is readily available and that the FDA's monitoring and approval processes for generic drugs are above reproach.

Thank you, Madam Chairman.

[The prepared statement of Ms. Col follows:]

AARP

**STATEMENT
of the**

AMERICAN ASSOCIATION OF RETIRED PERSONS

before the

**HOUSE SELECT COMMITTEE ON AGING
Subcommittee on Housing and Consumer Interests**

March 1, 1990

**Presented by:
Kathleen Col
Florida AARP/VOTE**

Good morning, Madame Chairman. My name is Kathleen Col and I am a Congressional District Coordinator for the AARP/VOTE program in Florida.

AARP is pleased to have the opportunity to discuss the problem that paying for prescription medications presents and the important role that generic drugs play in making medications affordable. While AARP strongly believes in improving consumer awareness about costs, benefits and potential risks associated with prescription medications; nevertheless, the responsibility for determining whether generic drugs are safe and effective must be borne by the FDA.

Prescription Drugs and Older Americans

Older Americans consume a disproportionately large share of prescription drugs. In the U.S., persons aged 65 and older represent only 12 percent of the population, yet they consume 30 percent of the prescription drugs. Further, because of financial circumstances, older people are less protected in this area than are younger members of the population.

In 1987, the mean number of prescribed medications per noninstitutionalized elderly Medicare beneficiary was 14.7--an increase of over 21 percent from 1980. Moreover, the mean expenditure per prescribed medication for this population was \$16.89 in 1987, up 110 percent from 1980. Finally, the mean

annual expenditure per individual on prescribed medications was \$248.10, a figure 154 percent higher than in 1980.

Within the elderly population, individuals between the ages of 80 and 84 consume more drugs, on average, than do older persons in other age groups. Of noninstitutionalized Medicare beneficiaries between the ages of 80 and 84, 88.4 percent had at least one prescribed medication in 1987. For this population with at least one prescribed medication, the average number of prescribed medications was 20.3 per individual.

Between 1980 and 1989, prescription drug prices rose by 128 percent, compared with an increase in the overall Consumer Price Index (CPI) of just over 50 percent. In 1989 alone, when the overall rate of inflation was 4.8 percent, average prescription drug prices rose by 8.7 percent.

The rate of increase in prescription drug prices between 1980 and 1989 (128%) is striking in that it has also exceeded the medical care component of the CPI over the same period (99%), a figure that has consistently and significantly outpaced the overall rate of inflation. In 1989, average prescription drug prices rose by 8.7 percent, compared to a medical care inflation rate of 7.7 percent.

Contributing to the sharp and frequent price increases for prescription drugs is the appearance on the market of high-priced

new drugs, the therapeutic effects of which are not significantly different from existing, lower-priced medications but which nevertheless drive up the prices of the older drugs.

Further, while three-fourths of all adults age 19 to 64 have insurance coverage for outpatient prescriptions, less than half of Americans over the age of 65 have such coverage. The private insurance coverage the elderly can obtain in Medigap policies is expensive and usually features substantial deductibles, coinsurance (e.g., 50 percent) and insurance policy limitations (i.e., a \$500 cap on what the policy will pay).

High prices, heavy utilization, and the absence of affordable coverage in the private Medigap marketplace have converged to make prescription drugs the second highest out-of-pocket medical expense for older people.

These high prices also affect the behavior of older Americans. According to a report by the Public Health Service, 15.5 percent of elderly patients who require prescriptions said that they are unable to pay for their drugs. Anecdotal accounts of older persons modifying their prescription drug regimens because of financial constraints are numerous. In 1986, an AARP national telephone survey found that the second most frequently cited reason given by older Americans for not getting a prescription filled as ordered by their doctors was the cost of the drug.

Since drugs are among the most cost-effective of medical care components, this increasing non-compliance with prescribed drug regimens may have the untoward result of increasing more costly physician visits or even hospitalizations. Inevitably, it also will contribute to misedication, already a serious problem among older Americans. According to an HHS Inspector General report, over a quarter of a million older adults were hospitalized in 1985 for adverse drug reactions. Thousands more suffer serious mental impairment as a result of inappropriate medication, and an estimated two million elderly are either addicted or at risk of addiction due to overprescribing of tranquilizers and sleeping pills. It is not surprising that the problem of over-medication and misedication has been dubbed by some as "America's other drug problem". The human cost of this problem cannot be measured and the financial cost of adverse drug reactions alone is estimated to be as much as \$7 million per year.

Generic Drugs and Public Confidence

Recent improprieties uncovered within the Food and Drug Administration and the generic drug industry have given rise to serious concerns about the integrity of the approval process for generic drugs. While it remains true that there has not been a documented report of an injury involving the use of any of the bioequivalent generic drugs approved since 1970, public confidence has been threatened.

In 1989 about one-fourth of prescriptions for non-institutionalized Medicare beneficiaries were filled with generic drugs. In general, the cost of generics is about 30-50 percent of their brand name counterparts. If confidence in these drugs declines, then people may be less willing to replace expensive brand name drugs with their more cost-effective generic counterparts.

In addition, declining confidence in generic drugs could have an effect on federal and state spending for health care. As taxpayers, we all pay more for brand name drugs through the state Medicaid programs.

The public must have confidence that all drugs, brand name and generic, meet the same rigorous FDA standards for purity, strength and quality. AARP has always urged patients to consult their physician with any questions about their medications, including the decision about whether to use a generic drug. This advice becomes even more important now.

AARP's Consumer Information Efforts on Prescription Drugs

AARP provides a number of sources of assistance on prescription drugs to its members. In 1989, for example, the Association conducted a survey of more than 1000 pharmacies in 42 states to learn more about drug prices. The results of the survey were published in August along with two new free AARP publications.

The Smart Consumer's Guide to Prescription Drugs features tips for older people on how to shop for the best pharmacy, information on generic drugs, and advice on using medicines safely. It also contains a medication schedule older Americans can use to better manage their medications. The second publication is called Consumer Pharmacy Surveys: A How-To Kit and contains the survey kit used by AARP volunteers in the more than 165 community surveys that made up the full report on drug prices.

Additionally, AARP's monthly news publication, the AARP Bulletin, with a circulation to all Association members, regularly addresses issues relating to prescription drugs. For example, recent articles have focused extensively on the generic drug industry, discussing topics such as a major federal investigation into the manufacturing, testing, and marketing of these products, and the FDA's tightening of its controls on generic drug approvals. Accompanying this statement, we are submitting for inclusion in the Record four articles on generic drugs published by the Bulletin between October 1989 and March 1990.

Further, AARP's Pharmacy Service implements a number of strategies to assist older people in the safe and efficient use of prescription drugs. All of AARP's pharmacies maintain readily retrievable records on prescription drugs, individual patient profiles, and sophisticated computer software on drug interaction. In addition, our pharmacies provide toll-free

telephone service to patients to assure easy access to a pharmacist when questions arise concerning medications. Moreover, AARP's pharmacies spend thousands of dollars annually on long-distance telephone calls to physicians, verifying medication orders.

One of the Pharmacy Service's most important initiatives, known as the Medication Information Leaflets for Seniors program (MILS), provides specially designed patient consultation information with each new prescription. MILS are informational leaflets for specific drugs. They inform the patient what the drug is, what it is used for, how to take it, what side effects to be aware of, and what questions to ask the prescriber. MILS also contain directions on how to store the drug and information the physician should know about the patient before prescribing a drug. MILS are developed with the assistance and cooperation of the Food and Drug Administration and leading geriatricians and pharmacologists. Currently, they cover over 500 drugs, representing 90 percent of the drugs AARP dispenses. The AARP Pharmacy Service also provides Braille labeling for the sight impaired and TDD telephone lines for the hearing impaired.

Finally, in 1988, the Pharmacy Service published the AARP Pharmacy Service Prescription Handbook. Prepared with the assistance of a panel of nationally known medical and health care experts, the 900 page volume is designed to provide expert information on the safe, effective use of the medicines most

frequently prescribed for persons age 50 and over. The book covers nearly 1000 drugs, offering comprehensive counsel on brand name drugs, prescription drugs, and over-the-counter medicines and vitamins, guidelines for drug administration, and all relevant precautions and warnings. It also includes a full-color 40 page chart for easy identification of hundreds of products by size, color, and shape.

Conclusion

Prescription drugs represent the second highest out-of-pocket medical expenditure among older Americans. Generic drugs which cost substantially less than their brand name counterparts provide some relief for those individuals facing burdensome prescription drug costs.

Recent revelations of improper practices by several generic drug firms as well as some FDA staff threaten public confidence in generic drugs. AARP is committed to improving consumer information about prescription medications, including generic drugs. AARP believes that the responsibility to ensure the safety and efficacy of generic drugs must be with the FDA. We look forward to continuing to work with members of this committee and the Congress to ensure that consumer information is readily available and that the FDA's monitoring and approval processes for generic drugs is above reproach.

p. 1

Feds launch generic drug probe

Corruption and fraud trigger major inquiry

BY BARBARA COLEMAN

Hunted by accusations of bribery and fraud, America's generic drug industry today faces a major federal investigation into the way it manufactures, tests and markets drugs.

While the charges have raised grave questions about government regulations and procedures used to guarantee the safety and effectiveness of generic drugs, there have been few suggestions that generics are unsafe.

Dr. Frank Young, commissioner of the Food and Drug Administration, the federal agency responsible for approving all prescription drugs before they can go on the market, put it bluntly:

"We have safety concerns, but we have not seen safety problems. And if we do, we will take that drug off the market."

Caught up in the charges are the FDA and a small group of drug manufacturers that make only about 18 percent of the 8,000 generics on the market. The firms are part of a relatively new industry that has burgeoned



in recent years as generic drugs have gained favor as a low-cost substitute for expensive brand-name drugs.

The scandal began last summer after three FDA chemists pleaded guilty in federal courts to accepting illegal gratuities from generic

drug makers. Presumably, the manufacturers wanted to speed up the approval process for getting new products onto the market.

Then, the FDA discovered an impropriety involving Vitarine Pharmaceuticals Inc.

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Generics

(Continued from page 1)

based in Springfield Gardens, N.Y.

It turned out that Vitarine had won approval of its own substitute for Dyazide, a widely used blood pressure medication, by stuffing test capsules with the brand-name drug, thereby assuring the two would pass laboratory tests for equivalency.

Suddenly, the entire industry found itself under a cloud. "This sorry spectacle shows the need for far better regulation than the generic-drug industry has received to date," says Rep. John Dingell, D-Mich., chairman of a House Energy and Commerce subcommittee that has been investigating FDA regulation of the industry for more than a year.

AARP supports an expanded inquiry. "A full and complete investigation is needed," says Executive Director Horace B. Deets, "to restore confidence in the generic drug industry, which has provided important cost savings, particularly for older Americans who might otherwise not be able to afford needed medications."

Responding to growing public concern, the Department of Health and Human Services, which has authority over the FDA, has announced a reorganization plan that will subject generics to more intensive review.

The FDA itself is asking Congress for greater authority to impose tougher penalties on drug companies found guilty of fraud. And, the agency is conducting a major investigation of the industry.

As part of that inquiry:

- FDA investigators have reported finding "significant problems" of misrepresentation, poor documentation or failure to follow FDA regulations by 11 of 13 companies that were part of an initial FDA probe;

- Twenty-nine generic products suspected of having won FDA approval

through improper procedures have been pulled off the market by two manufacturers;

- Another 141 generics are "under suspension," meaning that production of them has ceased pending completion of the investigation, although supplies already on pharmacy shelves can be dispensed;

- The FDA has broadened its inspections to include 20 of the leading generic drug manufacturers, along with a nationwide sampling and analysis of 30 generic products that represent three-quarters of all generics sold (see box on page 18).

Congressman Dingell says he is encouraged by the agency's response, saying it indicates "that the FDA is coming to grips with the problems."

At the same time, however, the legal counsel of Dingell's subcommittee, Reid Stuntz, warned: "If the problems are as widespread as they appear to be now, Congress will want to see more testing, more and better regulation and more and better enforcement."

As far as the generic industry is concerned, spokesmen say, it welcomes both the investigation and strict enforcement of the regulations that govern the manufacturing of its products.

The FDA's sampling program "will reaffirm that products in the marketplace are what they should be," says Dee Fensterer, president of the Generic Pharmaceutical Industry Association.

"We have no problems at all with increased oversight," adds Jacob Schein, president of Schein Pharmaceutical, Inc., one of the nation's largest generic drug firms. "The generic industry that comes out of this investigation will be a stronger industry."

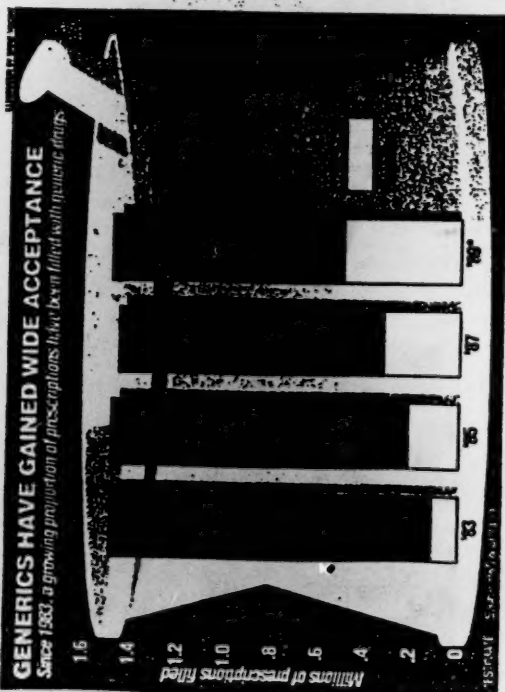
At the heart of the problem are the FDA's system for approving drugs and the procedures involved in implementing it. Critics say the FDA simply failed to establish procedures to prevent abuse. "Weak internal controls allowed

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In the eye of the storm: Rep. John Dingell (left) and FDA Commissioner Frank Young.



FIGURE 1



Generics

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 preferential treatment" for some drug firms, says a report by Inspector General Richard Kusserow of the Department of Health and Human Services.

Ironically, it was an FDA inspector making a routine check of a plant in the Virgin Islands who caught the manufacturer that put Dyazide into capsules and admitted them to the agency as a generic. Vitamine Pharmaceuticals has since admitted the fraud, and has with-

drawn the drug from circulation. Another generic copy of Dyazide figures in a dispute involving Bolar Pharmaceutical Co., a major maker of generics based in Copiague, N.Y. Bolar has asked a federal court to block the FDA from halting sales of its generic substitute for Dyazide.

So far the drug remains available at AARP's pharmacies, and elsewhere, pending Bolar's appeal for reconsideration. The FDA claims that a mixup in tests by Bolar in 1987 makes it unclear whether the drug actually passed muster. Bolar insists its product is both safe

and effective.

Part of the FDA's difficulty in carrying out its watchdog function may be due to the explosive growth of the generic industry. While generics have existed for a quarter century, they initially failed to emerge as a major market force. People didn't know about the drugs, and many generics faced a cumbersome approval process.

Then, in 1984, Congress passed the Waxman-Hatch Act, aimed at expediting the approval process as a way to hold down rapidly escalating costs of prescription drugs. Under the act, manufacturers seeking FDA approval must show only that their product is the "bioequivalent" of the brand-name drug it copies (see story on page 17).

Since then, what originally was a cottage industry has become so large and so profitable that even brand-name manufacturers have responded by making generic drugs.

Generics accounted for one third of all prescriptions filled in 1988. That year sales totaled \$3.4 billion, double pre-Waxman-Hatch receipts.

Crucial to the success of generic drugs has been the cost factor: Generics usually sell for a lot less than their brand-name counterparts. Indeed, a nationwide survey of prescription drug prices, conducted this summer by AARP volunteers, shows that generic drugs retail for about half the price of

the brand-name versions.

With the generic drug industry flourishing, economic pressures have intensified. And the competition has toughened. The way the industry works is that the generic manufacturer who gets his copy on the market first, after a patent expires on a brand-name drug, usually gains a competitive edge over those who come later. "The money," says Stuntz of the Dingell subcommittee, "is in getting the first approval."

And, it was in that high-pressure climate that three FDA chemists accepted bribes from manufacturers to speed up the approval process. "They were trying to get someone to move them up in the queue," explains former FDA Commissioner Jere Goyan, now dean of the School of Pharmacy at the University of California.

"It's a terrible, terrible situation," Goyan adds. "You have to get rid of people guilty of such infractions."

In all likelihood, says Dr. Ray Gifford, a Cleveland internist who is a trustee of the American Medical Association, the incidents of fraud and corruption that have come to light reflect only a "limited problem."

The danger, he adds, is that there will be "a panic reaction by the public," leading people to stop trusting drugs altogether. And that, says Gifford, would be a mistake, because "this country's record on drug safety is unequalled."

NO REASON FOR FEAR

Drug safety charges draw challenge

BY BARBARA COLEMAN

The debate over the safety of generic drugs heated up when a panel of the American Academy of Family Physicians cautioned doctors against prescribing generic drugs for persons over 75 and for people with illnesses such as heart disease, asthma or diabetes.

The panel's position was immediately challenged by many of the country's leading authorities on drugs. And government officials moved quickly to ease the concerns of consumers.

"We've had no reason to doubt the safety and efficacy of the vast majority of generics," says Dr. Peter Rheinwein, director of the Food and Drug Administration's (FDA) Office of Drug Standards.

The Academy's panel says that FDA testing of generic drugs has not proved conclusively that generics are equivalent to the brand-name products they copy. (The Academy represents 64,000 doctors.)

"FDA standards don't give us the assurances that we need" to believe generics are the same as brand-name counterparts, says Dr. Jerry Mann of Little Rock, Ark., chairman of the Academy's

Drug and Devices Committee, which drafted the group's report. "FDA needs to do more in the way of controlled clinical studies of generics."

The Family Physicians' report is based on a two-year review of medical literature, Mann says, and is independent of congressional and FDA investigations of the generic drug industry.

An independent expert, Peter Lamy, professor and assistant dean, geriatrics, of the University of Maryland School of Pharmacy, takes issue with the Academy. "There is no clear data that says generics are not safe and effective,"

clinical studies but on anecdotal material," says John McHugh, president of Retired Persons Services Inc., which operates the AARP Pharmacy Service. "In fact, the report presents no scientific evidence at all."

The organization's stance also drew immediate criticism from the generic drug industry. "Recycled, refuted allegations," says Dee Fensterer, president of the Generic Pharmaceutical Industry Association. "Generics have been on the market for a long time with not one instance of therapeutic failure," adds Robert Milanesi, executive director of the National Association of Pharmaceutical Manufacturers.

The heart of the debate: What constitutes "bioequivalency" between low-cost generic drugs and the brand names on which they are based?

The FDA does not require generic drug manufacturers to repeat the same broad clinical studies for safety and effectiveness that the originals must undergo to be approved for marketing. Generic drug companies must show only that they use the same chemicals or "active" ingredients as the original product and that their medications are absorbed at the same rate.

'In fact, the report presents no scientific evidence at all.'

JOHN McHUGH

Lamy says. "I don't think consumers have any reason to fear dramatic adverse outcomes" from generic drugs.

Other experts contend the Academy's study is seriously flawed. "The report's findings are not based on any

FDA rules allow generic drugs to contain different additives—such as binders, that hold a pill together, or fillers, coloring or preservatives—so long as these "inactive" ingredients do not significantly change the way the drug is absorbed into the bloodstream. The absorption level of most generics varies from brand-name counterparts as much as plus or minus 20 percent. "That variation hasn't proven to be clinically significant," McHugh says. "Even the brand-name product may vary within the same guidelines."

Even so, contends the Academy's Mann, that variation could spell trouble for a patient switched from a brand-name to a generic or even from one generic to another. The reason, he says, is that less of the drug may be absorbed or it may take longer to be absorbed. Elderly patients or those with certain illnesses are most at risk, he adds.

That argument draws some support from Dr. Ray Gifford, a trustee of the American Medical Association (AMA). Gifford, a Cleveland internist, says many doctors are cautious about generic substitution for patients with epilepsy or individuals who suffer from heart disease or irregular heart beats. He says these patients could be adversely affected by even slight changes in their medication.

But Gifford opposes the idea of a ban

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Safety

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ket ban on generics for older patients. "Whether you prescribe a brand name or generic depends not on the age of the patient," he says, "but on the condition you're treating or the drug you're using."

And other scientists say they don't think the additives in a generic drug will alter a drug's composition enough to cause problems for patients.

"Clearly people can have an adverse reaction to inert ingredients in a drug, but that's rare," says Dr. Brian Strom, associate professor of medicine and pharmacology, University of Pennsylvania School of Medicine. And, Strom adds, a brand name manufacturer may also change the additives in its products. Other experts note that the same brand-name manufacturer's products are different from batch to batch. So what should the public do when the experts disagree?

"Most physicians know when to prescribe generics and when they should insist on a brand name," says the AMA's Gifford. They should be taking cost into consideration, too, he says, particularly for older persons and those on fixed incomes, and adds:

"Patients should follow their doctor's advice."

FEBRUARY 1990

NEWSBREAK

AARP says recalled generic drugs are no threat to public

Recall of two generic drugs, including a widely used generic for treating high blood pressure, brought a cautionary note from AARP to its members: Don't stop taking the medicine without talking to your doctor, and don't panic.

ILLUSTRATION BY LARRY FORD



"This recall was not motivated by a danger or threat to the public health but paper documentation problems," says AARP.

Similar advice was issued by the Food and Drug Administration (FDA), which has been seeking recall of the medication, a version of the brand-name Dyazide, since last autumn. The FDA said it had not sought an emergency recall because there were no immediate or serious health threats.

Also involved in the voluntary recall by the manufacturer, Bolar Pharmaceutical Co., of New York, was

phenytoin, a generic version of the anti-epileptic medication Dilantin. The company said it hasn't distributed this particular generic since late last year.

In a statement, Bolar said, "These actions have been taken because the products' bioequivalence (to the brand-name products they copy) cannot be assured in the light of serious questions concerning the accuracy and reliability of the documentation" used in winning FDA approval to market them. The reference was to FDA allegations that there were numerous "discrepancies," "untrue statements," "errors" and "missing information" in safety-test results submitted by Bolar.

A process to force recall of the Dyazide generic was launched last November, and Bolar had resisted it until late January when a company lawyer notified FDA that an internal investigation had uncovered several falsehoods in Bolar's documentation.

The recall leaves consumers without a generic version of Dyazide, a SmithKline Beecham Corp. product for high blood pressure. On average, Dyazide costs almost twice as much as the Bolar generic.

STAMPING HONOR SYSTEM

FDA tightens its generic controls

BY BARBARA COLEMAN

Stung by criticism that lax regulation opened the way for corruption and fraud in the generic drug industry, the U.S. Food and Drug Administration (FDA) has begun tightening controls over generic drug approvals.

The FDA, which is responsible for approving all prescription drugs before they can be sold, says it plans to expand its audits of generic drug applications and increase inspections of generic drug company plants and the independent laboratories they use to test their products.

Nevertheless, says Neil Abel, an official in the FDA commissioner's office, "Generic drugs have been and

'Generic drugs have been and still are safe and effective.'

FDA'S NEIL ABEL

still are safe and effective."

Agency officials were expected to outline the new controls at a November hearing of a House Energy and Commerce subcommittee that has been investigating FDA regulation of the industry.

FDA officials say they will carry out the intensified reviews with doubling of the 80-person staff of chemists and inspectors in the recently revamped Office of Generic Drugs.

The process already has started, says FDA spokesman Michael Shaffer. "We're verifying and cross-checking the information we get from generic companies a lot more carefully."

The steps follow recent disclosures that several generic drug firms falsified data to win FDA approval of their products and that three FDA employees accepted illegal gratuities from generic drug companies.

"We're taking some positive steps to try to assure that this never happens again," says Abel. "We have ferreted out those companies that engaged in fraud and substitution."

Generic drugs are copies of brand-name drugs on which the patents have expired. They often cost half as much as brand-name counterparts because manufacturers need not repeat research and testing done on the original.

Problems arise in the industry, one

on an "honor system" for approving generics, accepting largely on faith test results submitted by the generic drug companies. And the companies had only to show their products were "bioequivalent" to their brand-name counterparts—that is, that they performed about the same in the bloodstream.

While generic manufacturers have been the focal point of the controversy, brand-name makers also have been accused of irregularities. The largest violator of FDA manufacturing standards was Eli Lilly & Company, a major brand-name firm.

Although the "honor" system is on its way out, some FDA critics say the agency still has a long way to go.

"They need a lot more cops on the beat," says Reid Strutz, legal counsel of the House subcommittee. "They're not as far along as they want to be, but then they're stretched in all directions."

Strutz adds that FDA officials "agree there are real problems. If they can't fix them, we'll have to try our hand at helping them."

The sweeping reorganization of the FDA's generic drug operation is part of a two-pronged effort to restore public confidence in FDA's ability to guarantee the safety and effectiveness of generic drugs. The other major step was a three-month investigation of 30 major generic drug products and 20 of the largest generic drug companies. Earlier, the agency had targeted 11 companies for special inspections because of specific allegations of fraud.

FDA officials say the investigation found less than 2 percent of 2,000 tested generic drug samples to be deficient largely in potency or dissolution. That rate is comparable, FDA officials say, to the rate the agency normally finds through regular inspections of brand-name and generic drugs.

A deficiency rating for dissolution or potency generally means, says FDA spokesman Shaffer, that the drugs in question do not dissolve properly in the stomach or don't contain enough of the major chemical in the original product.

FDA investigators also found evidence of manufacturing irregularities, fraudulent records or misrepresentation of products at several generic drug firms. One company, Viazine Pharmaceuticals, has admitted winning FDA approval for its copy of Dyazide, a blood pressure medication, by stuffing its capsules with the brand-name product.

Still, says Deputy Director Gerald Meyer of FDA's research center, "We don't think the nation's safety has been

Generic update

With a sweeping investigation of the generic drug industry almost complete, the Food and Drug Administration (FDA) says that only 1.6 percent of tested generic-drug samples have been found deficient in potency or dissolution.

That rate is similar to "normal industry conditions," the agency says.

The FDA says there is no evidence these particular generic drugs are unsafe, although they fall below the agency's standards for effectiveness.

The FDA inquiry, expected to be completed by mid-November, was triggered by revelations of bribery and fraud in the industry.

Ms. LLOYD. Thank you very much, Ms. Col. We appreciate your testimony.

Our next witness is Ms. Geraldine Brooks. We're happy to have you with us. I understand that you have over 15 years of accomplishment in public affairs in private and public sector administration. You certainly have a broad background to appear before us today. We're happy to have you.

STATEMENT OF GERALDINE BROOKS, RETIRED, WASHINGTON, DC.

Ms. BROOKS. Good morning, Madam Chairman and all participants and guests. My name is Geraldine Brooks, and I am currently retired on disability, living in Washington, DC.

I've been a diabetic since I was 12, and I am now diagnosed as legally blind, diabetic retinopathy; hypertensive, and a final stage renal patient on dialysis. I worked 36 years nonstop both here and abroad until 1986 when I began to lose my sight and began laser treatments. In 1987, I had surgery for a collapsed lung, followed by a seizure attributed to hypertension, and a drug interaction, followed by a heart attack in March of 1989. The kidney failure was diagnosed in May of 1989 and I began dialysis in August of 1989.

Several incidents in my life have brought me the belief that prescription drugs and the American medical practice are in a very sorry shape. Whether you are rich or poor, you take your life into your hands when entering a hospital and taking medications. Patients must monitor their own care, for Government monitoring has been ineffective. Better patient information is needed as well as a better mechanism to pay for the medications.

My first awareness of the problems with prescription drug pricing came when I worked as a narcotic inventory clerk after graduating high school. In one of New York's largest wholesale drug houses, I learned that the differential then between the manufacturer and patient cost was oftentimes 200 percent.

A second encounter with prescription drug problems was when I was Director of the National Minority Conference on Human Experimentation, sponsored by the National Commission for the protection of Human Subjects of Biomedical and Behavioral Research. Papers were presented on drugs and on the issue of prisoners and patients unknowingly being used as guinea pigs for drug manufacturers. Ironically, my mother died that same year as a result of having been prescribed a drug, chlorophenical, which had been recalled from the market 10 years prior. Although it had been recalled, 160,000 prescriptions were written each year.

One of the traumas of the my last 5 years has been that, while losing my sight, I was virtually blind for 3 months. Medications for my eyes were in containers the same size and shape as my nail glue. I could not see the instructions, the labels, or the patient warnings—a condition which continues and one which plagues all elderly people with vision problems.

In April 1989, I was discharged from the hospital after a heart attack with a long list of medications: nitro-patch, catapres, cardazen, digozin, insulin, sodium bicarbonate. The total cost was \$169. I

had many questions about the medications, but prescriptions were handed to me by a nurse upon discharge, and not by a doctor.

Over the next week, the medications seemed to be making me sick. I was unable to reach a doctor, and finally researched their effects myself in the "Physicians Desk Reference." I learned that the medications were fighting each other and that the digoxin on a daily basis can cause renal disorders. I went back to the hospital with digoxin poisoning, so ill that I had to be kept for 8 days. I believe that this poisoning accelerated my kidney deterioration, and I became a dialysis patient last August.

Whether prescriptions are for brand-name drugs or generics, health professionals who write prescriptions should be required to discuss the medications, their uses, the contraindications, and side effects with patients and in writing. DHHS, in its guide "Using Your Medications Wisely," has prepared helpful patient information charts on medication instructions and effects. Doctors and pharmacists should be required to use them. If generics are dispensed, it would be very helpful if labels stated the brand-name drug for which they were substituted. This would eliminate difficulties patients face when they try to remember which drug X is and how it should be used.

Generic drugs alone will not solve problems in affording medications. Because of my experience, I am very leery of taking generics when I am not absolutely certain of their equivalence. However, the two medications I now take—cardzen for high blood pressure at \$2 per pill, a monthly cost of \$200, and insulin at \$14 a bottle—have no generic equivalents. Why? It is interesting that high blood pressure medication, needed by so many people, and especially so many blacks, are some of the most expensive drugs on the market.

As I sit here today, I do not have the money to pay for my blood pressure medication. This only increases my stress. My medical condition is unchanging, but the Medicaid program is structured in such a bureaucratic way that people like me are bounced on and off every 6 months. During the gaps in coverage, needed drugs are extremely difficult to afford. I stretch my medications by taking them only half as much as I should.

As well meaning as these hearings are, it occurs to me that until there is serious monitoring of generic drugs, brand-name drugs, and the dispensation of such drugs, we will all be in danger of drug interaction deaths.

Thank you.

Ms. LLOYD. Thank you very much, Ms. Brooks. I certainly appreciate your testimony.

Ms. Col, we appreciate your testimony as well. For the audience, Ms. Col is congressional district coordinator for AARP's VOTE program in Florida. She is a congressional district coordinator; she's responsible for planning and implementing the election and legislative supportive activities in Florida's 19th Congressional District. We certainly appreciate your credentials and what you mean to AARP.

It is a very distinguished panel. Included in the panel is Ms. Cheryl Fish-Parcham, who is a case manager at Trinity Housing Community Family Life Services. She provides counseling and

social services to previously-homeless families now residing at traditional housing projects.

Certainly, we know that you give much of yourself, and it's a very worthwhile endeavor. I know in my area that homeless families are a big concern of mine, especially working for a program for women. So, I share your concern, and we are very anxious to hear from you.

STATEMENT OF CHERYL FISH-PARCHAM, ADVOCATE, LEGAL COUNSEL FOR THE ELDERLY AND COMMUNITY FAMILY LIFE SERVICES, WASHINGTON, DC

Ms. FISH-PARCHAM. Thank you for the opportunity to testify here today. I have worked for many years at Legal Counsel for the Elderly, a division of AARP which provides free legal assistance to the District of Columbia residents before beginning working in the transitional housing project, where I now work, for homeless families. I have encountered clients with great difficulties in affording prescription drugs in both positions. The problem is one which affects all ages.

Clients with chronic illnesses experience the greatest hardships. An elderly client of Legal Counsel for the Elderly today is waiting for a nursing home bed. Her monthly bills for prescription medicine total \$150, even though she is using generic substitutes for several medications. Because her medical bills are high, she qualifies for Medicaid in some months. However, because her income is above the poverty line, she cannot get Medicaid continuously. She must periodically spend down by showing that she pays the difference between Medicaid income standards and her own income for medical bills. During the months she is covered by Medicaid, she can get prescriptions filled with just a 50-cent copayment. However, during the months she is spending down, she must suddenly produce an extra \$150 for drugs and additional money for home care.

Ms. LLOYD. Would you explain this to some of us, the spending down issue?

Ms. FISH-PARCHAM. Many States have a medically-needy program in addition to the categorically-needy Medicaid program. The District of Columbia takes the option, under its categorically-needy program, to cover elderly people with incomes up to the poverty line.

The medically-needy program is to help people whose incomes are actually above these levels, but they consume the difference in medical costs. It's calculated over a 6-month period, and actually the spend-down program uses a lower-income standard. It's based on 133 percent of welfare benefits as opposed to the poverty line; it's a lower figure.

So, they calculate what is a person's income over 6 months compared to what is 133 percent of welfare benefits over 6 months. The person must show that they have incurred or spent that difference in medical bills before they're picked up by Medicaid. If it takes a person 2 months to do this, then they'll get Medicaid for the next 4 months, and then they'll start the process again. That's the same process that Mrs. Brooks was referring to.

Ms. LLOYD. Thank you.

Ms. FISH-PARCHAM. Unfortunately, this woman does not have the option of getting drugs and services now and paying for them over time. She must come up with all of the price of the medication before she'll receive coverage. The financial hardship and instability this causes have led her family to seek nursing home placement for her.

Unfortunately, the working poor experience similar problems. One family living in the transitional housing project where I now work consists of a woman working full time, a man disabled with asthma and diabetes, and four children. Though this family has limited health insurance, the family has no coverage for medicines.

Last week the husband showed me unfilled prescriptions for the following, and forgive my mispronunciations: zantac, about \$60; vanceril inhaler, proventil, and therodur, each between \$30 and \$45; diabinese, \$68; and deconannine, about \$40. Some of the prescriptions were several months old, for the family did not have the money to afford them. For this family, education about generic drugs could help. Although they thought they were getting the lowest-priced drugs, in fact, generics are available for three of the medications at about half the prices of brand-name medications.

Whether the family could afford even the reduced prices is another matter. The man has been taking expired doctors' samples of medicines until he can purchase more. Sadly, the expired medicine has not proven effective in controlling his blood sugar levels.

Besides educating consumers and monitoring the safety of generic drugs, the Federal Government should explore ways to restructure the Medicaid program to meet the prescription drug needs of the poor and the near poor. Right now the medically-needy population—that is, people whose incomes are above the poverty line but whose high medical expenses bring them within Medicaid eligibility limits—must show once every 6 months that they have paid or incurred enough medical expenses to qualify for Medicaid coverage of any remaining health bills.

Thus, a person with income of about \$800 per month must show \$2,500 worth of medical bills before obtaining Medicaid coverage. The \$2,500 is this patient's responsibility, but once this spend-down is met, Medicaid will pay any other covered health bills for the remainder of the 6 months. At the end of the 6 months, the person will need to show new expenses of \$2,500 before obtaining Medicaid again.

While such a Medicaid system may assist people with a large one-time expense, such as a hospital bill, it makes budgeting very difficult for people whose medical expenses must be paid monthly. A sliding fee scale premium, based on income, a monthly spend-down amount, would be much easier to comprehend, would in fact cost the Government no more money, and would allow people to space their own payments in order to afford prescription medications.

Thank you.

Ms. LLOYD. Thank you very much for your testimony. You brought out many features, many concerns that all of us have, and you've certainly enlightened me to the problems with the spend-

down provisions and what a hardship they cause. It seems rather unnecessary to me—

Ms. FISH-PARCHAM. It seems it to me.

Ms. LLOYD.[continuing] that they structure it that way.

Ms. Brooks, you have had a problem with your physicians and the pharmacists in making decisions as to which drugs you should take. Do you think this is prevalent among your friends, the people that you associate with; that this is not an isolated case, that this is pretty widespread?

Ms. BROOKS. Unfortunately, yes. Since I've been on dialysis, I have a dialysis community of people that I see very regularly. I'm among—I think I see 18 patients on a regular basis, three times a week.

The problem is threefold. Doctors don't seem to have the time to sit down and explain to a patient the medications and the possible side effects. They are not intelligent about the availability of generic drugs, and they write their prescriptions with reckless abandon, not considering the patient's condition.

Patients are intimidated, or are in such bad physical shape that they, themselves, don't seem to have any recourse. Pharmacists are not allowed in many areas to talk to patients about a prescription.

I was written a prescription for a drug called albanet. I took it to the drug store. It costs me \$89. Now this is a hypertensive drug for stress. The \$89 was enough to stress me. I went home and took the drug for 2 or 3 days. It may me psychotic, so I stopped taking it. And, guess what? I now have a bottle of \$89 worth of drugs that I cannot take back to the pharmacist; the doctor will not—there's no place for me to go. There's no way for me to get my money back. When you're on a fixed income, it really gets to be a problem.

The other thing that she didn't mention about Medicaid is that Medicaid not only wants you to prove that you're eligible, but they want you to do this 6 months in advance, the presumption being that there's a hospital, as in the case of a regular patient like myself, that's going to bill you 6 months in advance. I am not pregnant. None of my conditions are going to change. I'll be a diabetic; I will be a dialysis patient until I die. I'll probably have hypertension.

There is no way, no reason for the Medicaid system to say to me, "Ms. Brooks," every 6 months, "you can't be on Medicaid any more until you've proved to us that you're going to have medical expenses." I'm going to be on that machine for the rest of my life at a cost of about \$2,500 a week, and they know it. So how can I be over income? Nothing changes. My disability check stays the same. My illness either gets better or I die. But I have to go down to Medicaid and prance around and try to prove that I'm eligible for support.

It seems to me that there's something wrong in Denmark.

Ms. LLOYD. I think this should be a subject of another hearing of—

Ms. BROOKS. Yes, I'm sure.

Ms. LLOYD.[continuing] this problem, the lack of consistency in the Medicaid program.

Would you buy a genetic drug that you weren't as confident in simply because it was less expensive?

Ms. BROOKS. I might. I want to say that about generic drugs—AARP does a wonderful job of putting out wonderful materials. The materials that they put out, however, don't reach a large portion of the people that need to know about them.

Most of us, as I said, are so terribly intimidated when we go to the doctor. We don't question him.

My answer to the prescription versus generic drug thing is to try to get all kinds of natural, healthful things—meditate for my high blood pressure rather than fight it.

And why is there no generic drug for my high blood pressure? That is one of the most—

Ms. LLOYD. Isn't that the one that was—

Ms. BROOKS.[continuing] prevalent—

Ms. LLOYD.[continuing] called back? I think that was one that was called back.

Have you ever received any consumer booklets on advice, except for AARP, describing which generic drugs are available—

Ms. BROOKS. No, I have not.

Ms. LLOYD.[continuing] for older people?

Ms. BROOKS. No, I have never received any information. The information I've got from AARP I sought. The doctor didn't give it to me. The chart put out by DHHS that says what the counterindications of the drugs are, I sought it through AARP; it wasn't given to me by anybody.

Ms. LLOYD. Thank you very much.

Ms. Fish-Parcham, you described a client to us in very unfortunate circumstances with no drug coverage, and then almost complete coverage. Is this happening to poor people across America? Is this prevalent?

Ms. FISH-PARCHAM. It's prevalent. Some States have this spend-down program that I described; other States don't provide any coverage at all for the working poor, people who are above the poverty line, but it certainly is a prevalent problem.

Ms. LLOYD. Based on your information, what do poor people do when they simply do not have the money for the medication?

Ms. BROOKS. They don't take it.

Ms. FISH-PARCHAM. They don't take it.

Ms. BROOKS. They don't take it.

Ms. FISH-PARCHAM. And people suffer terrible health consequences.

Ms. BROOKS. And they get sick.

Ms. LLOYD. Aside from the human element that certainly we're concerned about or we wouldn't be in this room this morning, it seems to me that it's certainly more cost effective to give people their medicine and keep people out of nursing homes and keep them out of hospitals, not counting the suffering and saving lives and this dimension that we're concerned about. When you look at the practicality, certainly it's more cost effective to treat people for their illness and have them get well than to reach a condition where there's further debilitation.

Ms. FISH-PARCHAM. That's right.

Ms. LLOYD. Have you seen cases where your clients have been prescribed drugs that are duplicative or prescribed without suffi-

cient medical evaluation, such as Ms. Brooks reported; and that they're taking drugs that don't get along together?

Ms. FISH-PARCHAM. I have. I don't always know it until we begin investigating a disability case or something else. There aren't all that many professionals who will be interacting with a person to find out exactly what their medications are and what's wrong with them.

Ms. LLOYD. Do you think we need greater Federal assistance in providing prescription drugs?

Ms. FISH-PARCHAM. Yes, I very much do.

Ms. LLOYD. What role should the Federal Government play?

Ms. FISH-PARCHAM. I very much think that we do need more Federal assistance. I was sorry that the prescription drug add-on to the Medicare program didn't work, and hope that in Medicaid or some place else Federal assistance will take place.

Ms. LLOYD. Ms. Col, do you feel that there is not enough education to the patient from physicians and pharmacists? Should they pay a greater role in saying, "What medicines are you taking?" "Are you going to have complications because of the drugs that you're consuming?"

Ms. COL. Definitely. My husband is 87. He has Alzheimer's, so I'm very familiar with buying drugs and going to pharmacists and consider myself to be an informed consumer. I read all the books. I read the PDR. I check the drugs' act.

Many times I have had to go back to the doctor. He never tells what to do with the medication. He just writes a prescription very fast. I really don't have a chance to ask him, even though I don't think I'm an intimidated—I'm not being intimidated by him, but still he writes it out. I know in my mind I'm going to check him out anyhow.

But he's given my husband medication. My husband also has one kidney. Recent medication, when I looked it up, it said—I forget the exact term, but too much use of this will lead to renal failure. I called the doctor. I called the doctor back. He said, "Oh, well, we'll try another one."

I had the same situation as Mrs. Brooks. I could not take the medication back. I had bought it, unfortunately, and then got the instructions with the medication. The pharmacist, I think, should be required, as we do in AARP, to enclose a little informative booklet.

I would like to add, as Mrs. Brooks said she got the information from AARP—I know what we've done in Florida, and we do it throughout the country, AARP chapters. We don't just give this information to—we have booklets, as they say. We give these booklets out at all our chapter meetings. We have health fairs. I have personally conducted quite a few. We have all the booklets; anyone is welcome to pick them up. They're free.

I'm having a booth at a fair in Miami this month. We intend to have all the booklets, as many as people want, informing them on their drugs.

Ms. LLOYD. I want to thank you and commend you for what you're doing. We certainly appreciate your efforts and your concern and your love for your fellow man.

Does AARP believe that the FDA has taken the appropriate steps to insure that generic drugs are safe to older consumers since the crisis that's evolved?

Ms. COL. We believe that that is their role. It is up to the FDA to monitor it.

Ms. LLOYD. But do you feel that right now they've taken the appropriate steps to restore this confidence?

Ms. COL. I'm really not prepared to—

Ms. LLOYD. You're not prepared to answer that right now?

The American Academy of Family Physicians has concluded there are categories of patients and diseases for which generic substitutes should not be made. These groups include persons 75 years of age and older and females living alone with multiple diseases and multiple drug regimens. Do you agree with the Academy?

Ms. COL. That is one study. There were many, many studies.

Ms. LLOYD. But—

Ms. COL. As I say, I'm not prepared to answer that, either.

Ms. LLOYD. We thank you for your—we will submit some questions in writing to you for the record. I would appreciate it if all three of you would respond in writing. You've been wonderful witnesses, and I thank you very much.

[The following written questions were subsequently submitted to Ms. Col:]

1. Does AARP believe that the FDA has taken appropriate steps to ensure that generic drugs are safe for older consumers since the crisis at the FDA and in the industry?

2. The American Academy of Family Physicians has concluded that there are categories of patients and diseases for which generic substitutions should not be made. These groups include persons 75 years of age and older and females living alone with multiple diseases and multiple drug regimes.

Does AARP agree with the Academy?

3. I find the study that AARP has conducted regarding prescription drug purchasing to be very interesting.

Is it true that a brand name drug in one pharmacy can cost 22 times more than a generic version in another?

What kind of price variations occur for generics within a community?

4. MILS or Medical Information Leaflets seem to be a good way to inform consumers about specific drugs.

Do you think that such a product should be provided to all consumers?

5. Could we make the AARP publications on finding the best pharmacy, safe use of medications, and generic drugs entitled, "The Smart Consumer's Guide to Prescription Drugs" and "Community Pharmacy Surveys; A How-To Kit," available to persons who write to the Subcommittee?

Could we include these publications as a part of the hearing record?

[At the time this publication went to press, the American Association of Retired Persons had not responded to Chairman Lloyd's request for comments on these matters.]

Ms. LLOYD. Mr. James?

Mr. JAMES. Thank you.

Ms. Col, according to a recent news article, AARP has been involved in distribution of generic drugs, including some controversial ones. I think it's diazide which was recently recalled. Do you know anything about that at all?

Ms. COL. No, not really.

Mr. JAMES. Let me say, before I continue my questioning, I want to thank you all for your testimony. It's been very enlightening and very helpful.

Without your assistance, we can't get at all the facts. Maybe we'll never get at all the facts, but you've assisted us at getting at some of them, so we can make recommendations and understand the matters.

Ms. Col, AARP does dispense drugs, do they not, to their members?

Ms. COL. Yes—well, if people send prescriptions, they will dispense them, yes. It is a service of AARP. We have many services.

Mr. JAMES. It's a service?

Ms. COL. Yes, that's one of the services.

Mr. JAMES. Is there any profit at all connected with that?

Ms. COL. I really don't know. I have no idea. I know that my members—I used to be chapter president—would always send to the AARP pharmacy. They told me it was the cheapest. People do it for cost.

Mr. JAMES. But you don't know whether there's a profit. I assume there is no profit associated with it. You don't know?

Ms. COL. Well, we are a nonprofit organization, so I assume they are.

Mr. JAMES. I see.

Ms. COL. I really don't know. I'm just a volunteer.

Mr. JAMES. All right.

Ms. COL. I shouldn't say "just."

Mr. JAMES. That's correct. I want to compliment you for your volunteer—

Ms. COL. I used to say "just a housewife," and I stopped saying that.

Mr. JAMES. Do you know whether or not AARP helps with the problem Ms. Brooks was talking about by sending out when they do send their drugs out, a sheet that tells like a PDR does?

Ms. COL. Yes, they send a sheet. It's called a PILS. I'm not really sure—but it does tell them what the side effects, which I believe every person who receives a prescription drug should have a copy.

Mr. JAMES. Yes.

Ms. COL. It's very difficult to obtain. I know the AARP definitely does that. It's one of our—

Mr. JAMES. It does that with every—

Ms. COL. With every prescription.

Mr. JAMES.[continuing] with every prescription drug? Very good. It gives the side effects and—

Ms. COL. The side effects, has a warning when to take, what foods to take with, what not, what time—

Mr. JAMES. I take it all three of you would agree that it would be best that, if every time there was a prescription, there would be a paper that would give the side effects. It would give the generic version. It would give the popular or known name, so that you would be able to know what you were getting and to give the ingredients of it, along with obviously when to take it, how to take it, and the relationship to age, whether it's a child or an adult, and the conditions, the list of conditions, I would assume, that it may commonly be prescribed for?

Now I heard suggested in your testimony, Mrs. Brooks, that the physician should sit down and describe all these things but, regardless of anyone's economic status or relationship to the doctor, I'm sure all of us have found the same problem: that it takes a lot of the physician's time to sit down and describe all this. They could do that, I'm sure, but I might not be the solution in regard to the economics of the physician fees, if he only got to see 20 patients a day instead of the 50 or more. I would assume you would see a corresponding unacceptable increase as far as what we could all afford to pay in some cases.

But, in many cases that should be done and is done. I don't know to address that legislatively. Maybe we could figure out some way to make a recommendation, because all of us have experienced that difficulty.

Ms. LLOYD. At any age, if you're taking several medications, this can be a problem. I know some pharmacies advertise that they put everything on a computer screen. Of course, you have to buy all your medicines from one pharmacy. But, by doing so, they can have a complete scan of all that you are taking and advise you if there are counterindications.

Mr. JAMES. A lot of times a pharmacist can tell you a lot, but still you would like to have it from your physician's office if he's the one prescribing it.

The problem I have is they can tell you verbally, and I'll forget. I'll forget exactly what's compatible and what isn't. I'll forget unless it's all written out. The verbal explanation is fine, but I won't remember it 4 days later, especially and I imagine everyone has this problem—if I feel sick and I'm not in a frame of—or feel ill; I'm not in a frame of mind to retain much as far as the specificity.

I think it really would be helpful if we could get some way to encourage dispensers of it to do like the AARP does. It doesn't seem to me that that should be so expensive, to hand out a sheet with the instructions. Maybe there's a countervailing argument saying people would take it too literally.

I suppose one reason they don't is perhaps they're afraid of liability if they leave something out. I don't know. I don't know what all the complication are there.

Yes, Ms. Brooks?

Ms. BROOKS. In some States pharmacists aren't allowed to discuss anything about the medication that you receive. You're right about liability. I think that's a main issue. They just sort of leave it alone. They say they're not doctors and, if you want any information about your drug, you have to call your doctor.

Mr. JAMES. Yes, I think it's that way in many States, if not most. A lot of them want to tell you, but they're intimidated by those laws. "Wait a minute. I don't know why"—

Ms. BROOKS. They're concerned—

Mr. JAMES. That sometimes might happen, I'm sure.

Ms. BROOKS. They're concerned, if you knew what some of the side effects were, you wouldn't take the drug, and they're right. If you knew some of the side effects, you would not take the drug.

Ms. COL. May I say something? The drug that my husband is on right now, when I read the brochure that I insisted the pharmacist

give me—he did not give it to me; I had to insist on getting it—it said one of the side effects of this medication—it's called haldrog—is maybe sudden death, with no explanation.

Mr. JAMES. That would be one drug that I would have a tendency to avoid myself.

Ms. COL. It's haldrog or haloparadogs. That is definitely in one of the brochures, sudden death. No explanation.

Mr. JAMES. That would be intimidating.

Ms. BROOKS. Since it would be impossible—excuse me—for the pharmacist, the doctor, and everybody else to keep up with all of this stuff, perhaps legislation should be, could be initiated to have a monitor—and I'm not talking about the FDA, because obviously they have their hands full—a monitoring body or persons or a group that, in fact—whose responsibility it could be to get the information to the doctors and the pharmacist about the latest drugs or side effects.

In the case of my mother's drug, for instance, although that drug had been recalled, 160,000 prescriptions a year were written for that particular drug.

Mr. JAMES. That sounds fantastic and inexcusable to me that that would happen. It's hard to imagine, and I'm not—

Ms. BROOKS. And it was scandalized, and there was a big thing in The New York Times. I guess I would have had the basis for a class action suit, except that I promised her that I would never allow her body to be autopsied.

But, in fact, 160,000 a year were being given this drug that had been recalled 10 years prior. So maybe that's what is needed, is some sort of overseer, you know, that would get between me, the pharmacist, and the doctor, and insist that I get this written documentation that tells me what the possible, not only side effects, but interactions.

Mr. JAMES. I think that it may be that the health care professionals will welcome, quite frankly, a statute—

Ms. BROOKS. Sure, they would.

Mr. JAMES.[continuing] that would give very specifically what was required and thereby be a savings to them of liability. In other words, if they followed, then there would be a presumption of supplying the precise sufficient information, if you broke it out into specific categories: this is what you have to say and no more.

In other words, once they presume to give advice, it's also they have an intimidation if they leave out something, accidentally let's say, as far as what is required on the sheet. They may very well welcome—we would have to have some physicians and pharmacists and pharmaceutical companies testify as to the cost, because everything will be passed on to the consumer. So, whatever you pass—we've got a high cost of drugs right now. So, whatever we do, we don't want to do in such a clumsy manner as to add another 10 percent to the cost of our drugs. So that's why we have to be especially careful. Even though something is a good idea, we have to be sure that it's implemented appropriately, so as not to exacerbate the problem or increase the cost. We have that dual responsibility.

I will say that in some countries—I know we are not providing in many areas what we would all like to provide, and we have to examine it very carefully. But, there are some countries, for example,

that wouldn't provide dialysis after age 55. England, I believe, if I'm not mistaken, won't.

We do some things right, and I hope we can improve in every sphere and every aspect. There are 33 million uninsured people, I understand, in this Nation today, and that has to be brought to a halt. We have to redesign a system that will provide adequate health care, both drugs and otherwise, for all of us, whether or not we have income to pay for it. We must do that, and we will do it, I think, in the months and years to come. I hope soon enough.

Thank you so much for your testimony.

Ms. LLOYD. Thank you very much, Mr. James.

We're very happy that Congressman Pallone is with us. Thank you for being with us. Do you have any questions at this time?

Mr. PALLONE. No.

Ms. LLOYD. We appreciate your interest and your concern by being here today. And thank you, ladies, for your testimony. We really appreciate you. God bless you.

The Chair would now like to welcome Dr. Carl Peck from Washington who is Director of the Center for Drug Evaluation and Research with the Food and Drug Administration. We also are happy to have Mr. William F. Haddad from New York, who is chairman of the Generic Pharmaceutical Industry Association.

Gentlemen, we thank you for being here. We look forward to your very valuable testimony. Dr. Peck, you may go first.

STATEMENT OF CARL C. PECK, M.D., DIRECTOR, CENTER FOR DRUG EVALUATION AND RESEARCH, FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH AND HUMAN SERVICES, ROCKVILLE, MARYLAND; ACCOMPANIED BY: DR. DONALD B. BURLINGTON, ACTING DIRECTOR, OFFICE OF GENERIC DRUGS; DAVID G. ADAMS, ASSOCIATE CHIEF COUNSEL FOR DRUGS, GENERAL COUNSEL'S OFFICE; AND DANIEL L. MICHELS, DIRECTOR, OFFICE OF COMPLIANCE

Dr. PECK. With your permission, Madam Chairman, I'd like that three of my staff join me at the table.

Ms. LLOYD. Without objection, your staff may join you. If you'd like to introduce them to us, we would be happy to know who they are.

Dr. PECK. Good morning, Madam Chairman, Mr. James, Mr. Pallone, and absent members of the Subcommittee. We appreciate the opportunity to share with you the efforts of the Food and Drug Administration, and specifically the Center for Drug Evaluation and Research, to investigate the safety and effectiveness of generic drugs.

With me today, from the center, and counting from my left, is Dr. Bruce Burlington, M.D., Acting Director of our new Office of Generic Drugs; Mr. David Adams or our Chief Counsel's office; and Mr. Dan Michels of our Office of Compliance.

Ms. LLOYD. Thank you for being with us today.

Dr. PECK. I hardly need to point out that substantial public attention has been focused on generic drugs. Consequently, I will not attempt to restate in detail what has been stated in the media and at congressional hearings. But I would like to provide for the

record some of the information that has been provided to Congress and to the media during the past few months. I am hopeful that by providing this background information, I will be able to spend more time responding directly to the Subcommittee's concerns.

Ms. LLOYD. Without objection, your entire statement will be made a part of the record, and you may proceed.

Dr. PECK. In my judgment, the problems we are aware of at present with generic drugs are related to four events that occurred around the same time.

The first event was the disclosure that three of our former employees accepted money and other illegal gratuities from four generic pharmaceutical firms. I want to be absolutely clear that we consider what these employees did to be intolerable. Their actions were not only a violation of law, but also a violation of every professional and personal value that we believe in. We were angered and embarrassed.

Ms. LLOYD. Their greed has caused a great deal of suffering.

Dr. PECK. We feel a deep sense of betrayal, tarnish, and lowered esteem as a consequence of what was done and the publicity associated with it.

A second event, which appears generally unrelated to the gratuities, was our discovery that a small number of firms apparently decided that they could cut corners and submit fraudulent data as part of their premarking applications. In a few cases this involved a substitution of samples of the brand-name products for samples of their generic product in bioequivalence testing. In other cases it involved misrepresentation of manufacturing information and lot sizes for specific test batch records in the applications they submitted.

Such fraudulent and criminal behavior is repugnant. Quite frankly, we are utterly outraged by this behavior. What was once an honor system has been, at least temporarily, shattered. FDA's requirements are in place to assure that drug products will, in fact, be safe, effective, and uniform in content and quality. The fraudulent behavior of some firms jeopardizes that assurance and could place the health of some portion of the public at risk and ultimately undermine the integrity of an entire industry. Fraudulent behavior is wrong, and we are working hard to take action against it.

The third event that played a role in this matter emerged from our efforts to identify any further fraudulent submissions through inspections of select firms. This entailed detailed audits of manufacturing data. As a consequence of those detailed inspections, we became aware of a substandard level of good manufacturing practice compliance on the part of several generic drug firms. It is clear that some firms failed to meet the standards we regard as necessary to assure a safe and effective product, uniformity, and quality. Quite simply, this cannot be allowed.

The fourth event was a resolution passed by the American Academy of Family Physicians that expressed strong concern about generic drugs.

Whether these events are or are not closely related is not as important as what we have learned from this experience and the steps we have taken to correct the situation and prevent it from

happening again. The steps that we have taken thus far to prevent this from reoccurring are many and substantial.

In taking these steps, we have worked cooperatively with the House Energy and Commerce Subcommittee on Oversight and Investigations, the committee of Mr. Dingell; the United States Attorney's office; and our own Department's Office of Inspector General, all of whom have made substantial contributions to identifying and solving the generic drug matter. Among the more critical steps are the following:

First, the three FDA employees who have been charged and convicted to date that accepted illegal gratuities are no longer in Federal service. Any other employee who engages in criminal conduct will also be removed from the Food and Drug Administration instantly. I hasten to add that we do not believe this behavior was in any way characteristic of the more than 7,000 other dedicated employees at FDA. We have also undertaken to provide additional security and training intended to protect our employees from similar kinds of unethical and criminal practices in the future, and instruct them on how to handle any such attempts. Finally, we have instituted new practices to control and limit the access of drug company officials to FDA reviewers.

Second, we have identified the drug product applications reviewed by these three former employees, as well as those submitted by the four firms involved who offered the illegal gratuities, and have independently re-reviewed a number of them sufficient to satisfy ourselves that the product safety is not in question. These rereviews will continue as long as we believe they are necessary and useful.

Third, we have conducted a series of specialized inspections of generic manufacturers and bioequivalent testing firms. As part of this effort, over 2,800 samples of generic drug products and their brand-name equivalents have been tested for strength, potency, uniformity of content, and dissolution rate. In seven firms we identified applications that were based, at least in part, on fraudulent or questionable data. In every such situation we have requested a recall, changed that product's bioequivalent rating, and/or proceeded to withdraw marketing approval. We are also scrutinizing pending applications submitted by these firms. To date, approximately 63 products have been affected involving these seven firms. This is out of a total drug industry of around 8,000 to 9,000 products involving around 350 firms.

In another 12 firms we identified deviations from FDA's regulations concerning good manufacturing practices, which help assure the quality of drug products manufactured. In each case we have taken appropriate regulatory action. When warranted, this has included recall by the firm of existing products and our refusal to approve any new products that could be affected by the problem. I should note that problems with good manufacturing practice are not limited to generic drug firms. They are also periodically experienced in brand-name firms.

Fourth, we are studying the policies, procedures, and requirements associated with the manufacture and review of generic drugs to determine which changes are necessary to improve quality of

the product and ensure that the kinds of problems that surfaced over the past 2 years do not occur again.

We have met with major trade associations, solicited suggestions from a wide number of sources, and have begun to institute changes in our administrative and regulatory procedures and standards. We have reorganized and are recruiting and training additional staff. We are subjecting new and pending applications to an enhanced level of review by senior supervisors, and to review by our field staff. We are establishing an advisory committee to address scientific problems with particular products, such as those involving narrow therapeutic ranges. Further, we are developing a research agenda specifically directed at questions posed by generic drugs.

You will note in the testimony a paragraph here that relates to past and future anticipated fiscal requests. I will skip over that.

The steps we are implementing have slowed the review process for generic drugs. While we are concerned about this, the primary concern of the FDA must always be that the drugs that reach the market are safe and effective. I believe the steps I have described are necessary, and we will work as hard as we can to develop and put in place an improved process that both consumers and the industry can rely upon with confidence.

While we cannot provide you assurance that no more problems will arise, I want to make clear that at FDA will vigorously pursue legal, regulatory, and administrative penalties for those who submit false data or otherwise try to cut corners in the manufacture or review of pharmaceutical products. I believe that it is our responsibility to move quickly, decisively, and fairly in such situations, and I intend to honor that.

This brings us to the request outlined in your letter of February 9 and the central questions about generic drug safety and quality that I believe need to be answered for this Subcommittee and for the public at large.

The questions most often asked: are generic drugs safe and effective? What should consumers, pharmacists, and physicians do?

I continue to believe that currently marketed generic drugs are both safe and effective, and I want to underscore that. I take generic drugs myself, and I recommend them for my family.

We have roughly 10 generic drug products in my home. I have elderly parents. I'm on the phone with them at least once a week discussing their medications with them. Where we can, we use these generic drug products. We believe that they're safe and effective.

If and when FDA has reason to doubt the safety or effectiveness of a product, we will swiftly remove the drug or specific product lots that are suspect. We may also change the specifications for products we have reason to believe should be subject to different requirements.

Madam Chairman, we receive great volumes of data on drug applications and we investigate reports of product problems, defects, and alleged therapeutic failures for all drugs. The basis of our critical evaluation of that information, and on the advice of many outside experts, included among whom were 800 participants who joined us in 1986 for a scientific discussion on bioequivalency stand-

ards, it is our judgment that generic drugs as a class are safe and effective.

Where we could not longer ensure safety and effectiveness, we have taken, and will continue to take, decisive regulatory action to remove them from the market. We will continue to work diligently to maintain the safety and effectiveness of the generic drug supply.

I also have views about the responsibilities of physicians, pharmacists, and consumers. I believe that physicians should proceed as they always have in making sound diagnoses, making a judicious choice of treatment, and manifesting a commitment to monitor the therapy and the care of their patients.

I also believe that the moving testimony of Ms. Geraldine Brooks regarding the need for having their medicines explained to them by physicians and pharmacists is very compelling. The FDA provides highly-reviewed drug information in the package insert which should serve as a sound database for that counsel.

When it comes to a generic versus an innovator's brand-name product, I believe the decision is best left to the physician and the patient. There should be agreement between them, and I believe that a physician should be aware of which drug a patient is taking. If they jointly decide on a change in therapy, whether it be a switch between two brand-name products or between brand-name and generic, they should both commit to follow carefully the outcome of that change in therapy.

That advice is often included, by the way, in specific drug labels, even for switching—

Ms. LLOYD. If a patient goes to Doctor A and gets a prescription, and goes to Doctor B for another ailment, and doesn't tell Doctor B what Doctor A has prescribed, certainly there is no way that physicians can know that the patient has taken the drug that might conflict with the second drug.

Dr. PECK. You're very right. That problem in—

Ms. LLOYD. This seems to me to be one of the problems that we have here; that unless you tell your physician what drugs you're taking, then they can't know. So there's also responsibility of the patient to tell the pharmacist or the physician what they're taking.

Dr. PECK. I couldn't agree more. It would be handy if every patient always handed the physician they're interacting with a piece of paper that lists their current drugs.

Ms. LLOYD. I think this is a three-part responsibility.

Go ahead.

Dr. PECK. Agreed.

With respect to pharmacists, I believe that they should give careful attention to FDA evaluations of therapeutic equivalence, as outlined in our so-called "Orange Book," the approved drug products with therapeutic equivalence evaluations. It is a publication that is voluminous, information-rich, and that we publish each year and update frequently.

This will enable them to be certain that any substitution they make at a patient's request, and with the doctor's permission, is a substitution to a product that has an A rating, such as AA, AB, or AP. Such a rating signifies that the drug has been judged by the agency to meet the criteria of pharmaceutical equivalents, bioequi-

valence, labeling, and good manufacturing practice, and is, thus, considered therapeutically equivalent.

With respect to the consumers, I believe they should follow the advice of their physicians. I would urge consumers not to stop taking a generic drug that is working for them without discussing this with their physicians. Consumers should always consult their physician if they experience a problem with any pharmaceutical product, brand-name or generic.

Ms. LLOYD. Thank you very much.

Dr. PECK. I should add that, with the revelations of improprieties associated with generic drugs, it was clear to FDA's Office of Consumer Affairs that information regarding the safety and effectiveness of these drugs needed to be communicated to consumers in a timely and effective manner, as well as to maintain confidence in FDA's regulation of the industry.

Through its network of outreach activities, which has the capability of reaching 33 million consumers, FDA has disseminated six "Dear Consumer" letters on generic drugs, which encourage patients to continue to take generic drugs unless otherwise directed by their physicians.

Also, FDA's Office of Health Affairs has made a similar effort by distributing information on generic drugs to professional associations of pharmacists, physicians, and other health professionals. As information about generic drugs became available, it was sent, by telefax when urgent, to those groups.

Another avenue was the publication of a summary of FDA actions on generic drugs on the October 13, 1989 in an issue of the "Journal of the American Medical Association," widely read by physicians. We continue to use professional journals, participate in meetings, and give speeches to advise health professionals about general and specific aspects of generic drugs.

Madam Chairman, I want to conclude by assuring you that I agree with the societal judgment that Congress made when it said that there is a place for competition in the pharmaceutical marketplace without requiring repetition of expensive testing associated with the development of a new product. That's why we have a generic drug industry, and it's critical to both consumers and our Government, as everyone struggles with the cost of health care, to ensure the continued viability of this industry.

FDA is specifically charged with assuring the safety, effectiveness, and truthful labeling of our drug supply for both generic and brand-name products. We intend to faithfully carry out that mission.

Thank you for this opportunity to appear before you.

[The prepared statement of Dr. Peck follows:]



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

STATEMENT BY

CARL C. PECK, M.D.

DIRECTOR, CENTER FOR DRUG EVALUATION AND RESEARCH

BEFORE THE

SUBCOMMITTEE ON HOUSING AND CONSUMER INTERESTS

SELECT COMMITTEE ON AGING

U.S. HOUSE OF REPRESENTATIVES

MARCH 1, 1990

FOR RELEASE ONLY UPON DELIVERY

Good morning, Madam Chairman and Members of the Subcommittee. We appreciate this opportunity to share with you the efforts of the Food and Drug Administration to investigate the safety and effectiveness of generic drugs. With me today from the Center for Drug Evaluation and Research are Dr. Donald B. Burlington, Director of the Office of Drug Standards, Mr. Daniel L. Michels, Director of the Office of Compliance, and from the General Counsel's Office, Mr. David G. Adams.

I need hardly point out that substantial public attention has been focused on generic drugs. Consequently, I will not attempt to restate in detail what has been stated in the media and at Congressional Committee hearings. But I would like to provide for the record some of the information that has been provided to the Congress and to the media during the past few months. I am hopeful that by providing this background information, I will have more time to respond directly to the Subcommittee's concerns.

In my judgement, the problems we have experienced with generic drugs actually represent four events that occurred around the same time.

- * The first event was the disclosure that three of our former employees accepted money and other illegal gratuities from four generic pharmaceutical firms. I want to be absolutely clear that we consider what these employees did to be intolerable. Their actions were not only a violation of law, but also a violation of every professional and personal value in which we believe. We were angered and embarrassed. We feel a deep sense of betrayal, tarnish, and lowered esteem as a consequence of what was done and the publicity associated with it.

- * A second event, which appears generally unrelated to the gratuities, was our discovery that a small number of firms apparently decided they could cut corners and submit fraudulent data as a part of their premarketing drug applications. In a few cases, this involved the substitution of samples of the brand-name product for samples of their generic product in bioequivalence testing. In other cases it involved misrepresentation of manufacturing information and lot sizes for specific test batch records in the applications they submitted.

Such fraudulent behavior reflects, at a minimum, severely faulty judgement. FDA's requirements are in place to assure that products approved will, in fact, be safe,

effective and uniform in content and quality. The fraudulent behavior of some firms jeopardizes that assurance and could place the health of some portion of the public at risk and, ultimately, undermine the integrity of an entire industry. Fraudulent behavior is wrong and we are working hard to take action against it.

- * The third event that played a role in this matter emerged from our efforts to identify any further fraudulent submissions through inspections of select firms. This entailed detailed audits of manufacturing data. As a consequence of those detailed inspections, we became aware of a substandard level of Good Manufacturing Practice (GMP) compliance on the part of several generic drug firms. It is clear that some firms failed to meet the standards we regard as necessary to assure a safe and effective product of uniform quality. Quite simply, this cannot be allowed.

- * The fourth event was a resolution passed by the American Academy of Family Physicians that expressed strong concern about generic drugs.

Whether these events are or are not closely related is not as important as what we have learned from this experience and the steps we have taken to correct the situation and prevent it from happening again. The steps that we have taken thus far to prevent this from reoccurring are many and substantial. In taking these steps, we have worked cooperatively with the House Energy and Commerce Subcommittee on Oversight and Investigations, the United States Attorney's office and our own Department's Office of Inspector General--all of whom have made substantial contributions to identifying and solving the generic drug matter. Among the more critical steps are:

- * First, the three FDA employees that have accepted illegal gratuities are no longer in Federal Service. Any other employee who engages in criminal conduct will also be removed from the Food and Drug Administration. I hasten to add that we do not believe this behavior was in any way characteristic of the more than 7,000 other dedicated employees in FDA. We have also undertaken to provide additional security and training intended to protect our employees from similar kinds of unethical and criminal practices in the future, and instruct them on how to handle any such attempts. Finally, we have instituted new practices to control and limit the access of drug company officials to FDA reviewers.

- * Second, we identified the drug product applications reviewed by these three former employees, as well as those submitted by the four firms involved who offered the illegal gratuities, and have independently re-reviewed a number of them sufficient to satisfy ourselves that product safety is not in question. These rereviews will continue for as long as we believe they are necessary and useful.

- * Third, we have conducted a series of specialized inspections of generic drug manufacturers and bioequivalence testing firms. As part of this effort, over 2800 samples of generic drug products and their brand name equivalent have been tested for strength, potency, uniformity of content, and dissolution rate. In seven firms, we identified applications that were based, at least in part, on fraudulent or questionable data. In every such situation we have requested a recall, changed that product's bioequivalence rating and/or proceeded to withdraw marketing approval. We are also scrutinizing pending applications submitted by these firms. Approximately 63 products have been affected to date involving these seven firms. This is out of a generic drug industry total of some 8,000-9,000 products involving about 350 firms.

In another 12 firms, we identified deviations from FDA's regulations concerned with Good Manufacturing Practice, which help assure the quality of products manufactured. In each case we have taken appropriate regulatory action. When warranted, this has included recall by the firm of existing products and our refusal to approve any new products that could be affected by the problem. I should note that problems with Good Manufacturing Practice are not limited to generic drug firms. They are also periodically experienced in brand-name firms.

Fourth, we are studying the policies, procedures and requirements associated with the manufacture and review of generic drugs to determine where changes are necessary to improve product quality and ensure that the kinds of problems that surfaced over the past two years do not occur again.

We have met with major trade associations, solicited suggestions from a wide number of sources, and have begun to institute changes in our administrative and regulatory procedures and standards. We have reorganized and are recruiting and training additional staff. We are subjecting new and pending applications to an enhanced level of review by senior supervisors, and to review by

our field staff. We are establishing an advisory committee to address scientific problems with particular products, such as those involving a narrow therapeutic range. Further, we are developing a research agenda specifically directed at questions posed by generic drugs.

In order to continue to increase sampling of generic drugs, to certify that generic drugs are equivalent to brand-name drugs, and to conduct retrospective reviews of previously approved generics, the Administration has requested an FY 1990 budget supplemental of \$13.9 million. In FY 1991 we are requesting a total of \$45 million for generic drugs, an increase of \$10 million over the FY 1990 level (including the supplemental). Since the generic drug industry is only able to function if the public has confidence that generics are as safe and effective as brand-name drugs, we believe it is appropriate that the cost of maintaining this confidence should be borne by that industry. We are therefore requesting that FDA's generic drug budget be financed through user fees.

The steps we are implementing have slowed the review process for generic drugs. While we are concerned about this, the primary concern of the FDA must always be that the drugs marketed in this country are safe and effective. I believe the steps I have described are necessary, and we will work as hard

as we can to develop and put in place an improved process that both consumers and the industry can rely on with confidence.

While we cannot provide you assurance that no more problems will arise, I want to make clear that we at FDA will vigorously pursue legal, regulatory, and administrative penalties for those who submit false data or otherwise try to cut corners in the manufacture or review of pharmaceutical products. I believe that it is our responsibility to move quickly, decisively, and fairly in such situations, and I intend to honor that.

This brings us to the request outlined in your letter of February 9 and the central questions about generic drug safety and quality that I believe need to be answered for this Subcommittee and for the public at large.

The questions most often asked are whether generic drugs are safe and effective and what consumers, pharmacists, and physicians should do.

I continue to believe that currently marketed generic drugs are both safe and effective, and I want to underscore that. I take generic drugs myself, and I recommend them for members of my family. If and when FDA has reason to doubt the safety or

effectiveness of a product, we will swiftly remove the drug or specific product lots that are suspect. We may also change the specifications for products we have reason to believe should be subject to different requirements.

Madam Chairman, we receive great volumes of data in drug applications, and we investigate reports of product problems, defects and alleged therapeutic failures for all drugs. On the basis of our critical evaluation of that information and on the advice of many outside experts--included among 800 participants who joined us in 1986 for a bioequivalency workshop--it is our judgement that generic drugs as a class are safe and effective. Where we could no longer insure safety and effectiveness, we have taken, and will continue to take, decisive regulatory action to remove them from the market. We will continue to work diligently to maintain the safety and effectiveness of the generic drug supply.

I also have views about the responsibilities of physicians, pharmacists, and consumers. When it comes to a generic versus an inovator's brand-name product, I believe the decision is best left to the physician and patient. There should be agreement between them, and I believe that a physician should be aware of which drug a patient is taking. If they jointly decide on a change of therapy--whether it be a switch between

two brand-name products or between brand-name and generic-- they should both commit to follow carefully the outcome of that change in therapy.

With respect to pharmacists and providers of health care, I believe they should give careful attention to FDA evaluations of therapeutic equivalence, as outlined in our so-called "Orange Book" (Approved Drug Products with Therapeutic Equivalence Evaluations). This will enable them to be certain that any substitution they make at a patient's request, and with the doctor's permission, is a substitution to a product that has an "A" rating, e.g. "AA", "AB" and "AP". Such a rating signifies that the drug has been judged by the Agency to meet the criteria of pharmaceutical equivalents, bioequivalence, labeling, and Good Manufacturing Practice and, thus, is considered "therapeutically equivalent."

With respect to consumers, I believe they should follow the advice of their physicians. I would urge consumers not to stop taking a generic drug that is working for them without discussing this with their physician. Consumers should always consult their physician if they experience a problem with any pharmaceutical product--brand-name or generic.

I should add that, with the revelations of improprieties associated with generic drugs, it was clear to FDA's Office of Consumer Affairs, that information regarding the safety and effectiveness of these drugs needed to be communicated to consumers in a timely and effective manner, as well as to maintain confidence in FDA's regulation of the industry. Through its network of outreach activities, which has the capability of reaching 33 million consumers, FDA has disseminated six "Dear Consumer" Letters on generic drugs, encouraging patients to continue to take generic drugs unless otherwise directed by their physician.

Also, FDA's Office of Health Affairs made a similar effort by distributing information on generic drugs to professional associations of pharmacists, physicians, and other health professionals. As information about generic drugs became available, it was sent, by telefax when urgent, to these groups. Another avenue was the publication of a summary of FDA actions on generic drugs in the October 13, 1989, issue of the Journal of the American Medical Association. We continue to use professional journals, participate in meetings, and give speeches to advise health professionals about general and specific issues on generic drugs.

Summary

Madam Chairman, I want to conclude by assuring you that I agree with the societal judgement that Congress made when it said there is a place for competition in the pharmaceutical marketplace without requiring repetition of the extensive testing associated with the development of a new product. That is why we have a generic drug industry, and it is critical to both consumers and our government as everyone struggles with the costs of health care to ensure the continued viability of this industry.

FDA is specifically charged with assuring the safety, effectiveness, and truthful labeling of our drug supply, for both generic and brand-name products, and we intend to faithfully carry out that mission.

Thank you for this opportunity to appear before you. My colleagues and I will be pleased to answer any questions you or Members of the Subcommittee may have.

Ms. LLOYD. Thank you, Dr. Peck. I read your testimony last night and heard you again. I certainly appreciate your ability and your concern and the forthright manner in which you're handling these certainly unfortunate occurrences.

Mr Haddad is chairman of the Generic Pharmaceutical Industry Association; vice chairman of Schein Pharmaceutical Incorporated, a leading generic manufacturer. Mr. Haddad has been involved with the pharmaceutical industry issues since the Kefauver hearings in 1962, and as an aide to Senator Kefauver. You may have some Tennessee heritage here.

Prior to that, he was prize-winning investigative reporter and originally uncovered the story of the international tetracycline cartel in the early 1960s. We welcome you.

I was just told I think we're going to have to vacate this room in about an hour. So, I'm going to ask you, Dr. Haddad, if you would abbreviate your testimony, and your entire statement will be made a part of the record.

STATEMENT OF WILLIAM F. HADDAD, CHAIRMAN, GENERIC PHARMACEUTICAL INDUSTRY ASSOCIATION, AND VICE CHAIRMAN, SCHEIN PHARMACEUTICAL INC.

Mr. HADDAD. Thank you very much. I will abbreviate my statement. I was overseas and I faxed this, so I have some changes which I'll make for the record.

You asked me to address two questions: one, what can consumers do in this crisis, and how can they assure themselves about the safety, effectiveness, and interchangeability of generic drugs? Second, what has GPIA done about it?

The first I think was very effectively answered by Dr. Peck. I basically in my statement repeat some of the things that they have done.

When the 36,000 tests on 2,500 drugs was completed, Secretary Sullivan and Commissioner Young of the FDA announced in the name of the United States Government that the drugs in the marketplace were safe, effective, and interchangeable at that time.

Second, the results are historically consistent. Over 20 years the FDA has approved 9,000 clones of about 170 brand-name drugs without a single therapeutic failure.

Third, in every hospital, in every nursing home in this Nation generic drugs are used in rigidly-controlled and monitored circumstances. Again, they've never reported a documented failure. Chain drug stores, which fill millions of prescriptions every day and carefully monitor results, report no problems. The AARP, which dispenses more than 4.3 million prescriptions each year, 375 million dosage forms, reports no problems. That's convincing evidence.

But the truth of the matter is, as you know, there is a lack or a shaking of confidence in generic drugs. I have a paragraph in here that I don't have to read because I say that elderly have a double worry, as Senator Pryor and Congressman Waxman have found out over the years in hearings, that people have to choose between food and medicine.

Some of the things I heard today, frankly, scare the hell out of me. You can't stop taking a drug. You can't take a drug and imme-

diately stop; some you have to step down. You can't take half a drug. Like an antibiotic, you have to take the full 10 days or it doesn't do you any good.

The stories you've heard today have been heard for 30 years. Waxman-Hatch, that legislation, the Drug Price Competition Act set up a situation where people did not have to make that selection. Unfortunately, some people, because of lack of confidence in generics, have gone back to using brand-name drugs at much higher prices.

I want to make a couple of points here, and I they are related to what we're talking about. All drugs vary between different individuals, and so all drugs standards have certain tolerances. The allowed tolerances between a brand and a generic or a generic and a generic are based on the same tolerances that apply to brand-name products. Also, when a brand-name enters the marketplace, it goes through the same ANDA process as the generic drug.

It's become a virtual journalistic cliché that Waxman-Hatch reduced the requirements necessary for approval. That's absolutely false. I see it printed every day. What it did, if you'll permit me to be very frank, it tore a political Berlin Wall that was up between post- and pre-1962 drugs. The same procedures are used pre-1962 that are used post-1962 as a result of the legislation.

I talk about the Orange Book and the B-rated products, which are safe and effective, not interchangeable. We've campaigned to eliminate the B list.

I talk about what FDA calls a subpotent drug. You mentioned the drug diazide. Diazide was formed 17 years ago. You can formulate that drug with maybe a fraction of the active ingredient today. But in order to get to the marketplace with about 20 or 30 drugs, you have to formula back to the standards that were appropriate when the brand-name first came to market. That's a situation that has to be addressed.

More than half the generic drugs sold in America are sold by brand-name companies. Actually, generic companies make a lot of products for brand-name companies. For example, my company, we make products for five brand-name companies.

You can't tell a brand-name company from a generic company without a scorecard today. Lily, which is regarded as one of the highest esteemed brand-name companies, makes 600 generics. We're a large generic company. We make 300 generics.

Also, generic companies are going into new chemical entities, new variations on a form. The marketplace is getting mixed up. Two brand-name companies sit on my generic board and run generic companies.

I'm including in my testimony a sheet produced by the FDA which was sent to all the boards of pharmacy which addresses the arguments against generics. They call them myths. I think that might be useful for when you begin to promulgate the information that you are seeking.

What have we done about it? Well, first of all, "we" being the association, on two occasions prior to the Dingell investigation, we approached FDA with information about alleged favoritism, but we only had suspicions, no facts; smoke, no evidence, no fire. That evi-

dence was finally obtained by a generic company which brought it to Congressman Dingell.

Second—and I think the Dingell investigation has done a great service to our industry in the sense that it's helping us clean up a mess that many of us didn't know was there. When all this is done, for all the pain, I think that we'll be a stronger and better industry.

Second, over the years we have suggested various reforms in the FDA process. We've had a pretty good dialogue there. I've got some of those letters included for you to look at.

When fraud was established in the company, we booted them out of the organization. It's been a great financial sacrifice, great difficulty. We adhere to very strict legal standards. They either have to be proven guilty or admit guilt, and then they will bounce. I must say that the brand-name association, the PMA, does not do that.

We asked the FDA to undertake the narrow therapeutic study, the study of all the generic drugs in the marketplace, and also the white glove inspection of all the firms, which has been a real hardship for the good companies. They stay in firms about 5 weeks. They disrupt everything in process, but it has to be done. We requested it, and FDA has just about completed those investigations. They reveal some of the things that you've heard from Dr. Peck today.

We have a good working relationship with FDA. We're pleased at the direction they're heading. Obviously, we wish that they were going much faster, but I think the most important thing is the safety and effectiveness of drugs in the marketplace.

Next, we've created an unusual blue ribbon panel. We've asked the form head of the PMA, Lou Ingran, and a former FDA Commissioner, former FTC Commissioner, FPC Commissioner, three advisers to former Presidents, and also some of the best scientific talent in America to set up a committee, look at what happened, report back to us—not to us actually; to the American people. It's a totally independent operation financed by us. I'm not sure we'll agree with all their recommendations, but they will make those recommendations public.

We saw the flaw in the process that Dr. Peck talked about where a brand-name was submitted. We've taken voluntary action to close that loophole until the FDA publishes regulations.

To fully understand what is happening, however, we should place the generic scandal in its pharmaceutical context. All companies, brand and generic, have GMP problems. Lilly had its major plant closed and many of its products removed from the marketplace. The same was true for Abbott. One brand-name company accidentally mixed rat poison with a marketed product.

But I find it highly unethical for a brand company to cite an adverse reaction to a generic product and promulgate that information in the media, medical and general, without revealing that similar and expected adverse reactions occurred with their own products.

I think it's a credit to the PMA that not one PMA company was involved in the bribing of chemists at FDA for favorable treatment, although a number of brand-name firms are caught up in this investigation. It doesn't do anybody any good for the pharmaceutical

industry to have these kinds of investigations go on, but they're necessary.

I point out that several years ago 932 employees of the Veterans Administration had accepted gratuities and honorarium from five or six companies. The entire industry was not branded as being bad.

The same thing happens when you have a Oraflex, a Celegrin—drugs that—Dalcon Shield—that kill people. The individual company pays the penalty. Executives are fired. The company has lingering economic problems, but it is not a plague on the entire industry. I feel that it shouldn't be a plague on the entire generic industry.

What I am saying is that the innocent not be condemned along with the guilty, and a clear distinction be made between fraud and the routine problems of all pharmaceutical companies.

As you know, we have confidence in the FDA. We believe that the Dingell Subcommittee has spotlighted a crisis and created the impetus for change.

Something else is working out there right now. You ask me how to assure the elderly? The best way is through the pharmacist. The pharmacist is in the chain of command. He's the most trusted by anybody in the medical chain of command. They have wholesalers that are investigating us for quality. The buying groups investigate us for quality; the chain drug stores—and the pharmacist is in the middle of it.

I would personally recommend that you ask your pharmacist if the product that you're getting is the product that is safe, effective, interchangeable, approved by FDA, and comes from a good company. They live with it.

I differ slightly from Dr. Peck because doctors sometimes are too busy to do it. The first preference is the doctor, but the practical preference is the pharmacist.

Ms. LLOYD. But the pharmacist could get in trouble?

Mr. HADDAD. Not really. Not really. I think that the—

Ms. LLOYD. If he discusses the medication in a negative manner that the doctor prescribed?

Mr. HADDAD. For example, it's a working procedure that when you go in a pharmacy, you talk to the pharmacist. "Are there any side reactions to that?" "Is there a cheaper brand that I can get or less expensive brand?" "What happens?" "I'm taking another drug."

Pharmacists do that all day. The really community pharmacists, they have 5 years of training to do it. In medical school, unfortunately, they get a couple of courses on drugs and the education is picked up by the detail man, and the information from the brand-name companies, which is not always pure, which is somewhat economically tainted, although they do provide information.

I think, for example, when we repeal the anti-substitution law in New York, we put in a section that made it they wouldn't be liable for that.

I don't want to stand up here and appear to condone what went on. Thirty years of work went into getting competition in the generic industry. It started with Estes Kefauver, who was practically ruined in his political career, and went up to Congressman

Waxman and Senator Hatch. Those 30 years were filled with people who put their political careers on the line—the constituency, the elderly, the consumers, and others who stood out. A few greedy men—corrupt, greedy persons—in our industry and, unfortunately, in FDA have given everybody a black eye.

I think you deal with them. I think you deal with what the FDA is dealing with to make sure that everything that comes out is safe and effective. I think FDA has to err on the side of caution. I think the Dingell investigation will result in disclosures that will improve this industry. I think in the interim there is a role for this committee, and that is to get information, accurate information, out to the group that you serve so well, which is the consumer group through the various outlets.

The rest of it is in the testimony.

[The prepared statement of Mr. Haddad follows:]

Testimony of William F. Haddad

Chairman
Generic Pharmaceutical Industry Association
Vice Chairman
Schein Pharmaceutical Inc.

HEARING OF THE
SUBCOMMITTEE ON HOUSING AND CONSUMER INTERESTS
OF THE
SELECT COMMITTEE ON AGING
Thursday, March 1, 1990

My name is William F. Haddad. I am chairman of the Generic Pharmaceutical Industry Association and vice chairman of Schein Pharmaceutical Inc., a generic drug company.

You've asked me to address two questions today: are the generic drugs now in the marketplace safe, effective and interchangeable with their brand-name counterparts; and how has GPIA reacted to the current revelations about corruption within the FDA and within and by several generic companies.

Secretary Sullivan and FDA Commissioner Young answered the first question after conducting, following a request by GPIA, the most extensive survey ever undertaken by the Agency. Over 36,000 individual tests were conducted on 2,500 separate drugs which account for 75% of all the multi-source drugs dispensed in the market-place: the investigation found fewer problems (1.1%) than is usually uncovered in their random reviews of either brand or generic drugs in the marketplace (2%). With these results in hand, they assured the American people, in the name of the U.S. government, that generic drugs are safe, effective and can be safely interchanged with the brand-name counterparts. Those are the hard facts. Whatever else is reported is either uninformed speculation or economic propaganda.

Also, these results are historically consistent. Over the last 20 years FDA has approved some 9,000 generic clones of more than 170 brand-name drugs without a single...not one...documented instance of one failing to perform as the brand-name counterpart would have. This, despite massive efforts and expenditures of money by the self-named ethical drug companies to find such an instance. Let me repeat, not one such failure among 9,000 products used billions of times by patients over twenty years. The brand-name drug companies can not claim a similar safety record.

Three years ago the FDA invited 800 scientists to hear the complete litany of anti-generic arguments presented to an international panel of respected scholars in a full and open three-day hearing. The panel and FDA concluded after sixteen months of study that the arguments lack any legitimate scientific basis. In a report sent to all the state Boards of Pharmacy FDA concluded the anti-generic arguments were not scientific, but economic.

In addition, almost every hospital and nursing home in this country uses generic drugs in rigidly monitored circumstances. Again, they have never reported a documented failure. Chain drugstores, which fill millions of prescriptions every day and carefully monitor results, report no problems. The American Association of Retired Persons dispenses more than 4.3 million prescriptions each year -- 375 million dosage units -- and reports no problems.

Recent surveys within and without the pharmaceutical industry report an increase of 13% in generic dispensing at the pharmacy level (the first 10 months of 1989 vs a similar period during 1988).

Despite all this, what I fear has happened, and why this hearing is both so timely and so critical, is that the confidence of all consumers, and especially the elderly, has been shaken by the recent revelations of corruption.

The elderly have a double worry, as Senator Pryor and Congressman Waxman, have dramatically highlighted: they can not afford the increasing cost of pharmaceuticals and often must choose between medicine and food, between medicine and rent. The recent problems in the generic industry have already forced many back across the line, forced them to return to the terrible triage choices that The Drug Price Competition and Patent Term Restoration Act of 1984, Waxman-Hatch, was beginning to eliminate.

FDA has undertaken two other investigations following requests by GPIA: (1) a series of intensive inspections of the top generic and branded company manufacturing facilities and (2) a review of the so-called narrow therapeutic-range drugs. Also, approximately 1,500 test samples retained by independent testing laboratories are being checked against the marketed products. Two important points

need to be made here:

- (1) All drugs vary between differing individuals, and so all drug standards have certain tolerances. The allowed tolerances between a brand and a generic, or a generic and a generic, are based on the same tolerances that apply to brand-name drugs. Tighten up the brand tolerances and you tighten up the generic tolerance. Also, the underlying test generics must pass for marketing approval -- the bioequivalence test -- is based on the same procedure a brand-name product must pass before it can move from its investigative stage to a marketed product.
- (2) Although it has virtually become a journalistic cliché that Waxman-Hatch reduced the requirements for generic approval, that's absolutely untrue. For purely political reasons, before the new law, the successful process for approving generic versions of pre-1962 brand drugs did not apply to post-1962 drugs. It was a virtual Berlin Wall. The law merely removed that wall. No more. No less.

I would like to note that there are other anti-generic clichés which float in and out of the debate and which often become part of the dialogue:

- (1) The federal formulary, the list of interchangeable drugs, the

so-called Orange Book, contains "AB" rated, or safe, effective and medically interchangeable drugs, and "B" rated drugs which are safe and effective, but not interchangeable.

Frequently, these "B" rated drugs -- many of them, incidentally, are manufactured by brand name companies...are currently cited as being non-interchangeable, but not in the positive scientific sense; often used to "prove" to unsophisticated audiences that all generics are not interchangeable.

GPIA has actively campaigned to either upgrade or eliminate the "B" list, although the cost to some companies would run into millions of dollars.

- (2) Some brand-name drugs are what FDA classifies as "sub-potent". They were formulated with older technologies so, broadly speaking, a newer formulation of the drug can be just as effective as the older versions, but, for example, could be produced with only half the active ingredient, making safer and less expensive drugs possible. This could reduce the side effects for the elderly. USP or FDA could require these changes to be made in a way that would protect the innovator. GPIA has unsuccessfully urged this policy for many years, without success.
- (3) More than half the generic drugs sold in this country are sold by brand-name companies and a third of the ANDAs are awarded

to brand-name companies. But for over twenty years many of the so-called branded generics have been manufactured by generic companies for sale by brand-name companies.

Actually, some of the largest generic companies function as brand-name companies, and vice versa. For example, my company, Schein manufactures 300 immediate release and injectable generics; Lilly, one of the most outspoken anti-generic companies, manufactures some 600 generic, or off-patent, products.

The marketplace is also changing. Generic companies are and will continue to introduce new pharmaceuticals. As the saying goes, you can no longer tell a brand company from a generic without a score card.

I am including in my testimony a fact sheet prepared by the FDA for the State Boards of Pharmacy which labels most of the anti-generic arguments -- including the scientific tolerances theories -- as myths. The AARP has reproduced this report for some senior citizen organizations and GPIA has distributed it to the media, but these facts need wider circulation and I urge this Committee to consider that possibility.

Now what has GPIA done:

First, we had twice reported to FDA complaints from our Board of Directors about suspected favoritism by Dr. Charles Chang

towards Quantum and ATI. But we had only suspicions -- smoke -- but without evidence, no fire. That evidence was finally obtained by a generic company that hired a private detective.

Second, over the years we have suggested various reforms in the FDA process; I have included samples of that exchange. To insure a level playing field we need clear, consistent procedures and processes.

Third, when fraud has been established or admitted by a generic company we expelled them from our association. No parallel action has ever been taken against any Pharmaceutical Manufacturers Association member found to be filing fraudulent safety reports.

Fourth, we asked FDA to undertake the two studies of generic drugs I mentioned earlier and another of generic companies. The company inspections were the most rigorous ever undertaken by FDA and they usually lasted several weeks. For the innocent many that was a high price to pay for the guilty few. We were told similar white glove inspections would occur for the brand-name industry. They must take place to insure that all pharmaceuticals, not only generics, adhere to the Good Manufacturing Practices. I will discuss briefly below what some of those findings have revealed and what pending studies will reveal if the information we have is accurate.

Fifth, we have created a working relationship with FDA to provide information and advice on what the new Office of Generic Drugs needs to accomplish. We have suggested that some of the internal procedures we currently use to insure consistent quality be evaluated as possible future requirements for the entire pharmaceutical industry. We have proposed an ombudsman and enhanced enforcement.

Sixth, we created an independent Blue Ribbon Committee on Generic Medicines, which will function independently of GPIA and make public its findings and recommendations. The Committee is headed by a former President of the PMA, Lew Engman, and includes former FDA and former Federal Power Commissioners. On the Committee, in addition to scientists with unquestioned credentials, are advisors to three former Presidents of the United States. They will examine the current crisis, seek causes and make recommendations. The Committee has its own staff and will conduct interviews and may hold public hearings.

Seventh, a major flaw in the existing approval process enabled a company to submit for testing approval a product that was not its own, the so-called Vitarine situation. Incidentally, this incident was uncovered by Vitarine itself, which reported it to the FDA. We have made recommendations on how to close that loophole and, pending formal action by the FDA, GPIA members have voluntarily adopted those procedures.

To fully understand what is happening we should place the generic scandal in its pharmaceutical context. All companies, brand and generic, have GMP problems. Lilly had its major plant closed and many of its products removed from the marketplace. The same was true for Abbott and Lederle. One brand-name company accidentally mixed rat poison with a marketed product. I find it unethical for a brand name company to cite an adverse reaction to a generic product and promulgate that information in the media -- medical and general -- without revealing that similar and expected adverse reactions occur with their own products.

I also find it unethical for branded companies to repeatedly cite the allowable scientific tolerances of generic drugs without revealing that the same tolerances are allowed in their own products.

It is to their credit that not one PMA company, at the corporate level, has been accused of paying off an FDA chemist in this scandal for expediting its approvals (although one wholly owned generic subsidiary of a brand company was closed down and one person associated with a branded company gave small gifts to Dr. Chang). But previous disclosures about the sordid conduct of one or another brand company did not result in an industry wide condemnation.

A few years ago Congress declined to investigate the Veterans Administration when six branded companies gave gifts and gratuities to 936 (sic) employees...or to pursue instances where physicians working for brand name companies falsified or never conducted the studies reported to the FDA, studies which were critical to approval. Nor was the entire brand name industry castigated for Oraflex, Selacryn or the Dalkon Shield and other instances where critical scientific information was deliberately withheld and Americans died as a result.

What did happen was that these deviations from the norm were punished, and those companies and their executives suffered lingering economic problems. I am not trying to condone the illegal, unethical and abhorrent behavior of the generic companies who have violated and abused the public trust. They have and will pay their penalties under law and in the marketplace. I doubt if any of the guilty companies will survive in their current form.

What I am saying is that the innocent not be condemned along with the guilty and that a clear distinction be made between fraud and the routine problems of all pharmaceutical companies, brand and generic. We must carefully and diligently distinguish between arguments driven by logic and fact and those moved and motivated by and for economic gain.

The honest generic companies are now being severely damaged

by this crisis. For understandable reasons, FDA has all but stopped approving off-patent drugs, and by failing to approve routine supplements has created conditions which have frozen expansion in place, creating even greater economic hardships for the innocent than for the guilty who have paid light fines.

As you know, we have confidence in FDA. We believe the Dingell subcommittee has spotlighted a crisis and created the impetus for change.

Your letter asked for ideas on how to reassure the elderly. I believe the most successful and quickest way to do this, is to urge them to consult their pharmacist, the person they trust the most in the medical chain. The pharmacist and his wholesaler or chain or buying group has already sorted out the good companies from the bad, using knowledge, not rumors or propaganda, to make these decisions. They know which companies and which drugs -- brand or generic -- are in question. The marketplace is now doing what needs to be done. The customer can be reassured that his pharmacist is doing what is necessary to insure that the best quality products are dispensed.

The generic industry fought a thirty years war...between the investigations of Senator Estes Kefauver and the legislation of Congressman Waxman and Senator Hatch. We did not have plants strategically located or PACs to help with political access. In

1983 the brands had 90 Senators and two-thirds of the House sign-on for the patent extension legislation that would have all but ended competition in the pharmaceutical industry. We survived because of our arguments and our constituencies: the elderly, the consumers, the unions, and eventually, the media. The few greedy men who gave a black eye to our industry, betrayed the courage of the political leaders who supported us and the constituencies that gave us our strength. Their greed now threatens to deprive sick people of the medicine they need. We -- the GPIA -- is doing all it can to clean up the marketplace. FDA has in progress plans to create a level playing field. Secretary Sullivan and former FDA Commissioner Young have assured the American people their generic drugs are safe, effective and interchangeable with their higher priced brand-name counterparts. What is needed now is to get that message to the sick and elderly.

Thank you.

Ms. LLOYD. Well, I read your testimony last night, Mr. Haddad. I asked you to be brief, and I'm going to quote from your testimony something you didn't include.

"This greed now threatens to deprive sick people the medicine that they need," I hope that you're doing all that you can to clean up the marketplace. I commend you for your statement.

I think basically what both of you have said, we need to restore the confidence in the generic industry; that you feel that generic drugs are as safe as the brand-name drugs?

Mr. HADDAD. Yes, and they have to be carefully monitored by FDA. I can't say it; nobody would believe me. You have to have an independent authority like the FDA look at the drug, go through the scientific processes, inform everybody, and do a Secretary statement like Secretary Sullivan and Dr. Peck.

Now we don't know what the future will bring, but the drugs in the marketplace are safe and effective, to the best of FDA's knowledge. If they find something out, they can act very, very quickly. They need more authority than they have; they need more money, but basically Mr. Michels there, if he found something that he didn't think was right, you'd hear about it, and very, very quickly. You'd probably get about 4 hours to voluntarily do something about before you would step in if it was a serious kind of a problem.

But there is more enforcement authority needed, so that on the borderline cases FDA can move with—

Ms. LLOYD. Are both of you saying that we've had some bad players but the ball game should go on?

Dr. PECK. Essentially, yes. We are continuing our investigations. We're continuing a soupped-up monitoring of both incoming ANDAs and existing ones, but I certainly see no reason to shut the operation down.

Ms. LLOYD. Dr. Peck, are you completely confident that the remaining staff of the FDA involved in the processing of generic drug applications are not in any way violating the law, perpetrating fraud, or playing favorites to particular manufacturers?

Dr. PECK. To the best of my knowledge.

Ms. LLOYD. Do you expect more indictments?

Dr. PECK. I have no way of knowing whether there will be more indictments.

Ms. LLOYD. Are you confident that no companies are submitting fraudulent data or substituting samples other than their own drugs?

Dr. PECK. We have put in place much enhanced controls and critical review to assure that which include more onsite inspections, actual confiscation of or collection of samples that are tested, and extensive scientific testing to compare the two samples that were tested.

I believe that we are in a much enhanced position at the present time to guarantee that.

Ms. LLOYD. Well, are you confident that this wrongdoing is not going on now; that there aren't more greedy men out there?

Dr. PECK. Well, as I say, to the best of my knowledge, within the agency, I have no reason to suspect that any current FDA employ-

ees in the review chain are doing or have performed any illegal acts.

The generic drug industry is a somewhat more difficult question to answer, and I'm going to ask our Director of Compliance, Mr. Michels, to give you an idea of what the level of surveillance that we have been able to attain so far—

Ms. LLOYD. Very good. I think that's what we really want to hear.

Dr. PECK.[continuing] and what his views are.

Mr. MICHELS. Thank you, Madam Chairman.

I guess maybe I should say, for starters, that there will always be a need for the Food and Drug Administration because we live in an imperfect world.

Ms. LLOYD. Well, I don't care what your profession is, there will always be greedy people out there.

Mr. MICHELS. Exactly. Exactly.

We've embarked on a number of major activities. As Dr. Peck indicated in his testimony, we've been focused—have had very intensive, focused inspections on a small number of suspect firms and a somewhat larger number of generic firms to determine the scope of the problem.

It's been despicable, but we have found instances of fraud. Dr. Peck has spoken to the significance and impact in the ultimate marketplace; that is, what we've seen thus far, this represents a relatively small proportion. But, because we're not omnipresent, we can't guarantee that in any one particular location there might be a firm or an individual who might be cutting a corner or submitting fraudulent data to us.

Right now we are in the process of overhauling our field inspectional programs to close any element of the honor system. This will apply to both abbreviated new drug applications—i.e., generic products—as well as brand-names, because the opportunities for fraud exist in both areas.

When we have fine-tuned and put in place those programs, we will have much more intensive inspection and surveillance, and we will, as the opportunity presents itself, for cause and on a random basis, go back and look at previous applications.

What I can tell you is that we have uncovered a number of problems. They have taught us and led us in the direction of how to prevent these problems from occurring in the future. Very strong effort and aggressive action is being taken.

Ms. LLOYD. I want to make it very clear that I think this is a very, very serious crime—not only to give, as you said, Mr. Haddad, give the industry a black eye, but to frighten older people that need medicine. There are people that are not on the medications that they need because of this fraud and this abuse of trust.

I think that certainly there should be severe penalties. What do you think is an appropriate penalty, Dr. Peck, for a company that defrauds the Federal Government and the American people?

Dr. PECK. Well, that's a question that I'm not very well prepared to answer.

Ms. LLOYD. Do you think they should be allowed to continue to produce drugs?

Dr. PECK. Absolutely not. When we discover fraudulent behavior, which utterly shatters our trust and confidence in a company's capacity, to submit information to us that we can evaluate, it just basically, totally crumbles our capacity to be confident in them.

So—

Ms. LLOYD. Go ahead.

Dr. PECK. It is a complex problem, however. These are often large concerns with multiple manufacturing sites or multiple products. If there's been a focal defect in a particular plant involved in one individual or one product, that's a different matter from a widespread, multisite corporate behavior pattern.

Ms. LLOYD. The 7 firms that you identified, or the 12 that deviated, will they be prosecuted?

Dr. PECK. I'd like to ask our general counsel here to answer that. I think he has more specific information on that.

Mr. ADAMS. Actually, we're not in a position to discuss further prosecutions at this time, by agreement with the Department of Justice.

Ms. LLOYD. With the Justice Department?

Mr. ADAMS. They've asked us not to discuss specifics.

Ms. LLOYD. I would expect that at this time.

Well, can you tell us, Do you think they'll be capable of producing safe drugs in the future? Do you think that the isolation of employees leaves them in a position to move forward?

Dr. PECK. Well, I'd like to refer back to the comments I made earlier. It will depend upon the extent of the corruption within the company.

Ms. LLOYD. It will be a case-by-case judgment.

Dr. PECK. There is one company you know in which the extent of problem has become so pervasive that the company has essentially shut down distribution of all of its drug products.

Ms. LLOYD. I'm going to have some more questions for you that I'm going to submit in writing. But, I would like you, for the record, to just give us a list of the companies that you mentioned in your testimony.

Dr. PECK. Yes.

Ms. LLOYD. And the six of your consumer letters on generics for the hearing record, if you would?

Dr. PECK. Yes, Ma'am.

[The following material was subsequently received:]



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

JUN 27 1990

The Honorable Marilyn Lloyd
Chairman, Subcommittee on Housing
and Consumer Interests
Select Committee on Aging
House of Representatives
Washington, D.C. 20515

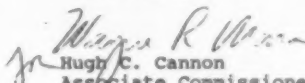
Dear Ms. Lloyd:

This is in response to your March 21, 1990 letter which followed your hearing of March 1, concerning generic drug safety. We sincerely regret the long delay in responding.

Enclosed is a memorandum from Carl C. Peck, M.D., Director of the Center for Drug Evaluation and Research, which contains responses to your questions, as well as requested documents.

We will make every effort in the future to provide our responses more promptly. Please thank your staff for their patience.

Sincerely yours,


Hugh C. Cannon
Associate Commissioner
for Legislative Affairs

Enclosures

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: JUN 26 1990

FROM: Director, Center for Drug Evaluation and Research, HFD-1

SUBJECT: Response to Representative Lloyd's Letter of March 21

TO: Associate Commissioner of Legislative Affairs, HFW-1

This is to respond to Rep. Lloyd's letter of March 21 regarding the generic drugs hearing. Below are her questions and my responses to questions one through five. Attached you will find the material requested in questions six and seven: the list of companies and the six "Dear Consumer" letters on generic drugs that I mentioned in my testimony.

1. In your testimony, you referred to fraudulent behavior as "at a minimum" a "severely faulty judgement."

Are you implying that this behavior was simply a mistake or was their behavior reprehensible to the FDA?

Response:

In no way was my characterization of fraudulent behavior as "at a minimum" a "severely faulty judgement" intended to suggest that this behavior was a simple mistake. I try to avoid overstating issues, but be assured that I find this behavior absolutely reprehensible.

- 2 -

2. Given your inspections, do you believe that the generic drugs produced by companies that have been convicted of fraud and have withdrawn products from the market are capable of producing safe drugs regardless of their mistakes?

Response:

FDA has not concluded that the generic firms that submitted fraudulent data are incapable of producing safe drugs. The Agency has investigated the issue of fraudulent data, and all products that have been associated with fraudulent data have been removed from the market. FDA also conducted inspections, product analyses, and application rereviews for other products of firms who submitted fraudulent data. Further, the drug firm employees who were identified as being associated with these instances of fraudulent behavior have been removed from the firms or reassigned to activities in no way related to the drug review process. Based on these activities, the data we now have supports the safety, effectiveness, and overall quality of the products on the market that have not been associated with fraudulent submissions.

3. Would a supplemental appropriation be helpful in hastening the FDA's reorganization, training, and restaffing?

Response:

A supplemental appropriation would be helpful in hastening the FDA's reorganization, training, and restaffing as it relates to the agency's generic drug program activities. The Administration transmitted a supplemental request for such resources with the 1991 budget. We understand it has been favorably reviewed and passed by the House and the Senate, and we hope conference action will be completed in the near future. Any help they can provide to facilitate passing the appropriation would be greatly appreciated.

4. Do you have the necessary facilities to handle increased staff? If not, what do you need?

Response:

The necessary facilities, or space, to handle increased staff has been a severely constraining factor. While the primary problem is office space sufficient to accommodate increased staff, there is an identifiable need for associated laboratory and clinical facilities to address questions which are not the province of a specific manufacturer, or which involve issues that are contested between different manufacturers.

- 3 -

The Public Health Service has recently signed a lease for office and laboratory space for our Division of Anti-Viral Drug Products. FDA requested the space on April 19, 1989. The General Services Administration (GSA) advertised for the space on June 12, 1989, and the lease was signed on April 19, 1990. We are currently scheduled to occupy the office space on August 4, and the laboratory space in October.

Also, the FDA is in the process of obtaining additional office space for generic drug review needs. PHS requested 60,000 square feet on April 18, 1989 and GSA advertised for the space on June 12, 1989. FDA first requested space to accommodate growth in November 1987 and adjustments increasing the requests were made on August 24, 1988, September 26, 1988, and December 18, 1988. GSA made three announcements for a lease signing, in February, April, and June of this year, but the lease has not yet been signed. FDA will occupy the space 120 days after a lease is signed. The space was originally scheduled to be occupied in February 1990. The current estimate is November.

Finally, 2,500 square feet of space has been obtained for pre-clinical laboratory studies at FDA's Shady Grove, Maryland complex on an emergency lease basis. FDA requested the space on April 24, 1989. The space did not have to be advertised, because the request was small enough for a sole source contract. A lease was signed October 16, 1989, and FDA occupied the building October 27, 1989.

In addition, the Agency is in the process of requesting proposals for collaborative agreements to work with a local medical school in the development of some limited clinical capability.

5. What actions has the FDA taken to force the generic firms, that you say failed to meet good manufacturing practice standards, to assure safe and effective products?

Response:

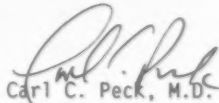
In each case where significant departures from Current Good Manufacturing Practices (CGMPs) are found, the management of the firm involved is informed of the deficiencies and advised of the corrective actions that are necessary. In six cases to date involving generic firms, regulatory letters were sent requesting replies within 10 days and informing the firms of potential legal action if corrections were not accomplished.

- 4 -

If defective or otherwise unsafe drugs are found to have been marketed, FDA also seeks recall from the marketplace. Among the generic firms investigated, six of them have recalled a variety of defective products (not including the recalls of products associated with fraud).

Also, and perhaps of primary importance, no new drug applications, abbreviated new drug applications, requests for procurement by Federal agencies, or certificates to foreign governments are approved for products affected by deficiencies unless and until the firm involved is brought into compliance. Follow-up inspections are made to assure that corrective action is accomplished and maintained. If corrections have not been made or do not continue, FDA will use all remedies provided under law, such as seizure and injunction, to assure that compliance with GMP is achieved and maintained.

I hope these responses and the enclosed material will be helpful. I would also like to convey my appreciation to Representative Lloyd for her interest in our program.



Carl C. Peck, M.D.

Enclosure

Firms found to have given illegal gratuities to former FDA employees:

American Therapeutics, Inc.
Par Pharmaceutical Basics, Inc.
Quad

Those found to have submitted fraudulent ANDAs:

American Therapeutics, Inc.
Bolar
Chelsea
Par
Quantum
Superpharm
Vitarine

Those found to have significant deviations from good manufacturing practice or ANDA commitments:

Barre-National, Inc.
Bolar
Par
Pharmaceutical Basics Inc. (one plant)
Pharmafair
Quad
Vitarine
Watson
Biocraft (one plant)
Lederle (one plant)
Sidmak

FDA's evaluation of these and other facilities is ongoing. Some of these firms have already corrected the problems; examples: Watson; Sidmak. None of the firms in the first group (fraud) are considered in-compliance at this time.



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

JAN 9 1990

Dear Consumer:

Once again, we take this opportunity to provide information on the latest developments in FDA's review of generic drugs. This review is part of a 6-point plan of action initiated by FDA, in cooperation with the Department of Health and Human Services, to ensure an adequate supply of safe and effective generic drugs.

Enclosed is a list of generic drug products which have been the subject of FDA suspension, recall, or withdrawal actions. As of December 29, most actions have been taken to recall certain drugs or to withdraw the Abbreviated New Drug Applications because the assurance of bioequivalency was lacking. Other reasons for action included misrepresentation of formula or batch size, discrepancies in records, and failed dissolution.

FDA is recommending that consumers of generic drugs continue to take their medication unless advised differently by their doctors or pharmacists.

Sincerely yours,

Alexander Grant
Associate Commissioner
for Consumer Affairs

Enclosure

Week ending: 12/29/89
 GENERIC DRUG PRODUCT SUSPENSION, RECALL AND WITHDRAWAL ACTIONS

MANUFACTURER	DATE	PRODUCT	TYPE OF ACTION	REASON
American Therapeutics Bohemia, NY	8/3/89	Triamterine/Hydrochloro- thiazide Tablets, 75mg/50mg	Recall D-224-9	Failed dissolution test
	12/27/89	Prednisone Tablets 5 mg, 10 mg, and 20 mg	NOOH to withdraw ANDAS to be published	Lack of assurance of bioequivalency
	12/27/89	Clonidine HCl Tablets 0.1 mg, 0.2 mg, and 0.3 mg	NOOH to withdraw ANDAS to be published	Lack of assurance of bioequivalency
	12/27/89	Lorazepam Tablets 0.5 mg, 1 mg and 2 mg	NOOH to withdraw ANDAS to be published	Lack of assurance of bioequivalency
olar opiaque, NY	11/2/89	Nitrofurantoin Macro- crystalline Capsules 50mg and 100mg	Recall (D-015/6) and NOOH to withdraw ANDA to be published	Lack of assurance of bioequivalency
	11/2/89	Triamterine and Hydro- chlorothiazide Capsules, 25mg / 50mg	NOOH to withdraw ANDA to be published	Lack of assurance of bioequivalency
ar Pharm oring Valley, ,	10/4/89	Leucovorin Calcium Tablets, 5mg and 25mg	Recall D-005/6-0	Manufacturing record discrepancies
	8/1/89	Megestrol Acetate Tablets	Recall D-235-9	Lack of assurance of bioequivalency
	10/16/89	Orphengesic Forte Tablets	Recall D-234-9 and NOOH to withdraw ANDA	Lack of assurance of bioequivalency

MANUFACTURER	DATE	PRODUCT	TYPE OF ACTION	REASON
Pharm. (continued)				
	10/16/89	Orphenesic Tablets	Recall D-233-9 and NOOH to withdraw ANDA	Lack of assurance of bioequivalency
	10/16/89	Triamterine and Hydrochlorothiazide Tablets, 75mg/50mg	Recall D-232-9 and NOOH to withdraw ANDA	Lack of assurance of bioequivalency
	10-18-89	Dipyridamole Tablets 25mg, lot 9C756	Two lots recalled (D-017-0)	Failed dissolution
	9/7/89	Decon Decongestant SR Tablets	Recall D-244-9	Failed Dissolution
	9/7/89	Dexchlorpheniramine Maleate Tablets, 4mg	Recall D-245-9	Failed dissolution and stability testing
	10/6/89	Dexchlorpheniramine Maleate Tablets, 6mg	Recall D-004-0	Failed dissolution
	10/18/89	Dipyridamole Tablets 25mg, lot 622388 and 626388	Recall D-017-0	Failed dissolution

MANUFACTURER	DATE	PRODUCT	TYPE OF ACTION	REASON
Quantum Pharm. Amityville, NY	10/20/89	Clorazepate Dipotassium Tablets, 3.75mg, 7.5mg, 15mg	Recalls D-056/8-0	Lack of assurance of bioequivalency
	10/20/89	Diazepam Tablets, 2mg, 5mg, and 10mg	Recalls D-059/61-0	Lack of assurance of bioequivalency
	10/20/89	Doxepin HCl Tablets, 10mg, 25mg, 50mg, 100mg, and 150mg	Recalls D-048/53-0	Lack of assurance of bioequivalency
	11/02/89	Fenoprofen Capsules, 200mg and 300mg	Recalls D-072/3-0	Formula misrepresentation
	10/20/89	Lorazepam Tablets, 0.5mg, 1mg, and 2mg	Recalls D-062/4-0	Lack of assurance of bioequivalency
	10/20/89	Meclofenamate Sodium Capsules, 50mg and 100mg	Recalls D-065/6-0	Lack of assurance of bioequivalency
	10/20/89	Minoxidil Tablets, 2.5mg and 10mg	Recalls D-046/7-0	Lack of assurance of bioequivalency
	11/02/89	Oxazepam Capsules, 10mg 15mg and 30mg	Recalls D-069/71-0	Batch size misrepresentation
	11/02/89	Timolol Maleate Tablets 5mg, 10mg, and 20mg	Recalls D-075/7-0	Quantity produced does not reconcile with raw
	10-25-89	Nystatin Vaginal Tablet, 100,000 units lot 8901915	Regulatory letter issued 10/25/89 - Recall D-079-0	Subpotent

MANUFACTURER	DATE	PRODUCT	TYPE OF ACTION	REASON
Quantum Pharm. (continued)				
	10-25-89	Nystatin Vaginal Tablet 100,000 units, lot 8919301	Regulatory letter issued 10/25/89 - Recall D-079-0	Subpotent
	10-25-89	Nystatin Oral Tablet 500,000 units lot 8835618	Regulatory letter issued 10/25/89 - Recall D-078-0	Subpotent
	10-25-89	Nystatin Oral Tablet, 500,000 units lot 8832705	Regulatory letter issued 10/25/89 - Recall D-078-0	Subpotent
	10/20/89	Trazodone HCl Tablets, 50mg and 100mg	Recalls D-054/5-0	Lack of assurance of bioequivalency
	11/02/89	Triamterine / Hydro- chlorothiazide Tablets, 75mg / 50mg	Recalls D-074-0	Batch size misrepresentation
Superpharm Bayshore, NY	10/25/89	Chlorthalldone Tablets 25mg and 50mg	Suspended	Missing or discrepant records
	8/8/89	Diazepam Tablets 2mg, 5mg, and 10mg	Suspended	Discrepancies in record
	11/15/89	Ibuprofen Tablets, 400mg	Suspended	Discrepancies in test records
Vitarine Springfield Garden, NY	10/3/89	Baclofen Tablets 10mg and 20mg	NOOH to withdraw ANDA	Lack of assurance of bioequivalency

MANUFACTURER	DATE	PRODUCT	TYPE OF ACTION	REASON
arine (continued)				
	10/3/89	Cephalexin Capsules 250mg and 500mg	NOOH to withdraw ANDA	Lack of assurance of bioequivalency
	10/3/89	Cephalexin Oral Susp 125mg/5mL and 250mg/5mL	Recall D-178/9-9 and NOOH to withdraw ANDA	Lack of assurance of bioequivalency
	10/3/89	Cephadrine Capsules, 250mg and 500mg	Recall D-177-9 and NOOH to withdraw ANDA	Lack of assurance of bioequivalency
	10/3/89	Clindamycin HCl Capsules, 75mg and 150mg	Recall D-174/5-9 and NOOH to withdraw ANDA	Lack of assurance of bioequivalency
	10/3/89	Desipramine HCl Tablets 10mg	Recall D-154-9 and NOOH to withdraw ANDA	Lack of assurance of bioequivalency
	5/26/89	Desipramine HCl Tablets 25mg, 50mg, 75mg, and 100mg	Recall D-155/158-9	Lack of assurance of bioequivalency
	10/3/89	Desipramine HCl Tablets, 150mg	Recall D-159-9 and NOOH to withdraw ANDA	Lack of assurance of bioequivalency
	10/3/89	Doxycycline Hyclate Capsules, 50mg and 100mg	Recall D-163/4-9 and NOOH to withdraw ANDA	Lack of assurance of bioequivalency
	10/3/89	Indomethacin Capsules, 25mg and 50mg	Recall D-167/8-9 and NOOH to withdraw ANDA	Lack of assurance of bioequivalency
	10/3/89	Indomethacin Extended Release Capsules 75mg	NOOH to withdraw ANDA	Lack of assurance of bioequivalency
	10/3/89	Meclofenamate Sodium Capsules, 50mg and 100mg	Recall D-169/70-9 and NOOH to withdraw ANDA	Lack of assurance of bioequivalency
	10/3/89	Mefenamic Acid Capsules, 250mg	Recall D-160-9 and NOOH to withdraw ANDA	Lack of assurance of bioequivalency

MANUFACTURER	DATE	PRODUCT	TYPE OF ACTION	REASON
Mitarine (continued)	10/3/89	Orphenadrine Compound Tablets, Single and Double Strength	Recall D-165/6-9 and NOOH to withdraw ANDA	Lack of assurance of bioequivalency
	10/3/89	Tetracycline HCl Capsules 250mg and 500mg	Recall D-161/2-9 and NOOH to withdraw ANDA	Lack of assurance of bioequivalency
	5/26/89	Triamterine and Hydrochlorothiazide Capsules, 50mg/25mg	Recall D-176-9 and voluntary withdrawal of ANDA	Lack of assurance of bioequivalency
	10/3/89	Triamterine and Hydrochlorothiazide Tablets 75mg/50mg	NOOH to withdraw ANDA	Lack of assurance of bioequivalency
	10/3/89	Trimipramine Maleate Capsules, 25mg, 50mg, and 100mg	Recall D-171/3-9 and NOOH to withdraw ANDA	Lack of assurance of bioequivalency
Merrimack Pharmaceuticals, Inc., OH	9/13/89	Dipyridamole Tablets 25mg, 50mg, and 75mg	Recalled (D-253/255-9) (25mg lot 80031)	Failed dissolution
		Conjugated Estrogen Tablets, 0.625 mg lots 8884, 8538, 8536, and 8975	Recalled	Failed content uniformity
Emmon Co. Sellersville, PA	9/14/89	Nystatin Vaginal Tablets 100,000 units, lot 6092	Recalled (D-260-9)	Subpotent

MANUFACTURER	DATE	PRODUCT	TYPE OF ACTION	REASON
Chem everport,	10-31-89	Thyroid Tablet 3gr, lot 2953	Recalled D-068-0	Failed assay
	10-31-89	Thyroid Tablet 1gr, lot 3169	Recalled D-067-0	Failed assay
ra. Basics ver, CO	9-27-89	Nystatin Oral Tablets 500,000 units lot G343-03	These lots plus 13 other lots recalled (D-001-0)	Subpotent
	9-27-89	Nystatin Oral Tablets 500,000 units, lot G257		Subpotent
	9-27-89	Nystatin Oral Tablets 500,000 units, lot G489-02		Subpotent
	9-27-89 ¹	Nystatin Oral Tablet, 500,000 units lot G576-03		Subpotent

NY 1 - Sample was collected in follow-up to an out-of-specification Top 30 Drug Sample analysis

MANUFACTURER	DATE	PRODUCT	TYPE OF ACTION	REASON
Index Calipharma) Elizabeth, NJ	11-13-89	Prednisone Tablets 5mg, lot 9M517	UDL recalled lot 11/13/89	Failed dissolution
Locraft Labs Wood Park,	12/1/89	Chloroquine Phosphate Tabs 250 mg, Lot 14311	Recalled D-090-0	Foreign tablets in bottles
Itual Pharm ila., PA	5/5/89	Verapamil Hydrochloride Tablets, 80mg	Recall D-124-9	Failed content uniformity
dmak Hanover,	12-5-89	Dipyridamole Tablets 25mg, lot 0180173	Recall D-088-0	Failed content uniformity
	12-5-89	Dipyridamole Tablets 25mg, lot 0580798	Recall D-088-0	Failed content uniformity
	12-5-89 ¹	Dipyridamole Tablets 25mg, lot 0190236	Recall D-088-0	Failed dissolution
	5/12/89	Poly Vitamins with Fluoride, chewable tablets	Recall D-147-9	Subpotent for vitamin D
	10/17/89	Dipyridamole Tablets 25 mg, lot 0680920	Recalled	Failed content uniformity

KEY

1 - Sample was collected in follow-up to an out-of-specification Top 30 Drug Sample analysis

MANUFACTURER	DATE	PRODUCT	TYPE OF ACTION	REASON
Kare-National Baltimore, MD	5/26/89	Bromanate Elixir, 4oz	Recall D-138-9	Mislabeled
	5/26/89	Dimenhydrinate Syrup 16oz and 1 gallon	Recall D-135-9	Crystallization of active ingredient
	5/26/89	Fluocinalone Acetonide Topical Solution	Recall D-137-9	Subpotency
	7/5/89	Flurandrenolide Lotion	Recall D-236-9	Unapproved manufacturing procedures
	7/5/89	Hydrocortisone Lotion	Recall D-237-9	Stability data does not support expiration dating
	5/26/89	Promethazine with Codeine Cough Syrup, lots 82565 and 82636	Recall D-136-9	Incorrectly labeled
	7/5/89	Theophylline Syrup	Recall D-238-9	Lacks preservative
	7/5/89	Triacin-C Cough Syrup	Recall D-239-9	Labeled potency is wrong



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NOV 20 1989

Dear Consumer:

You will be pleased to know that the Food and Drug Administration, after nearly completing an exhaustive study of the generic drug industry, has found no evidence to date indicating that generic medications now in use pose a serious public health threat.

In his testimony before the House Subcommittee on Oversight and Investigations on November 17, FDA Commissioner Frank Young discussed some of the findings of the "Interim Report on Generic Drugs." He reported that the Agency inspected 36 generic drug companies and analyzed more than 2,500 samples of the top 30 generic drugs; they represent about three-fourths of the new generic prescriptions filled each year. FDA found that 98.9 percent of the samples checked complied with requirements for purity, potency, and uniformity of content and dissolution. This rate is comparable to that of the drug industry as a whole.

Commissioner Young and Dr. Louis Sullivan, Secretary of the Department of Health and Human Services, have announced a six-part action plan designed to prevent similar problems in the future: intensified analyses of generic drugs and firms; reorganized and strengthened drug review procedures; establishment of an independent ombudsman reporting directly to the FDA Commissioner; closer cooperation with the office of the HHS Inspector General; new legislation to strengthen and clarify authority to act promptly against any improper activity in connection with drug approval applications; and alternative methods of financing to supplement the corrective actions taken thus far.

We would appreciate any comments you may have on the report, as well as any reactions you receive from your constituents. You may send them to Dr. Rose Britanak, Room 16-85, Office of Consumer Affairs, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857. If you would like a complete copy of Dr. Young's statement, contact Dr. Britanak on (301) 443-5006.

Sincerely yours,

Alexander Grant
Associate Commissioner
for Consumer Affairs

Enclosure

AN INTERIM REPORT
ON GENERIC DRUGS

UNITED STATES FOOD AND DRUG ADMINISTRATION
ROCKVILLE, MARYLAND
NOVEMBER 17, 1989

An Interim Report on Generic Drugs
United States Food and Drug Administration
November 17, 1989

Part One: A Brief History of Generic Drugs

Before Congress passed the Pure Food and Drug Act of 1906, the most appropriate advice for people using drug products was caveat emptor--let the buyer beware. The free market was essentially that: there was no effective regulation of drug products sold in the United States, and no assurance that they were effective or even safe.

The 1906 law gave the U.S. government the authority to remove unsafe drug products from the market, but it also placed on the government the burden of proving that a drug was unsafe. It was not until 1938, with passage of the Federal Food, Drug and Cosmetic Act, that drug products were required to demonstrate their safety before they could legally be marketed. Proof of a drug's efficacy before marketing came as recently as 1962, with the enactment of the Kefauver-Harris amendments to the Food, Drug, and Cosmetic Act.

Thus, after 1962, all drugs approved had to be shown to be safe and effective for their intended uses. As more and more of these so-called "post-1962" drugs gained approval, it became

apparent that a new public policy question would soon need attention: what would happen with the expiration of the patents for these new drugs?

Many health policy experts advocated increased competition in the pharmaceutical marketplace by encouraging the availability of "generic" copies of brand name prescription drugs--that is, competing versions of brand-name drugs whose patents have expired. Increased competition, it was argued, would reduce the future costs of these "multi-source" drugs and help ease spiraling health care costs.

And yet there was no consensus on the best way to achieve that end. Some questioned whether the Food and Drug Administration (FDA) even had the authority to approve generic drugs. By the late 1960s, the FDA had begun to review requests to manufacture generic copies of brand-name drugs first approved before 1962, and it developed an "Abbreviated New Drug Application" (or ANDA) for that purpose. These abbreviated applications contained information on product formulation, manufacturing, and quality, but they did not include the clinical safety and effectiveness data required of innovators to show that the active ingredient worked. This process greatly reduced the cost of drug approval.

FDA also created a "Paper New Drug Application" process,

whereby a firm could rely on published studies to demonstrate the safety and efficacy of their generic copy of brand-name drugs first approved after 1962.

Nevertheless the FDA lacked explicit statutory authority to approve--through the ANDA process--generic copies of brand name drugs approved after 1962, and there were questions about what criteria would be sufficient for approval of such products. In response to these issues, Congress enacted the "Drug Price Competition and Patent Term Restoration Act of 1984." This law has two purposes: to foster innovative pharmaceutical discoveries through patent extension, and to increase competition in the generic drug arena, thereby making lower cost generic drugs more widely available. The law authorizes FDA to accept ANDAs for generic versions of all brand name drug products, including those approved after 1962, and set forth criteria for approval.

Not surprisingly, passage of the 1984 law greatly increased the number of ANDAs submitted to the FDA: more than 1,000 in fiscal year 1985 alone. Since October, 1984, nearly 5,000 have been received, and more than 2,000 have been approved.

Along with the increased work load created by the flood of ANDAs came increased pressure to approve drugs quickly. Within the generic drug industry, there is a perception that the first firm

to receive FDA approval for a given drug will reap a long-term market share advantage over later firms marketing other versions of the same generic drug.

The economic stakes are high. During 1988, sales of generic drugs in the U.S. totaled \$3.4 billion. Annual sales of generics are expected to reach \$9 billion by the early 1990s. Furthermore, generic drugs now account for nearly one-third of all new prescriptions filled by pharmacists.

There is also evidence that the public policy of encouraging competition has successfully generated cost savings. Generic drugs are usually less expensive than brand name drugs; the American Association of Retired Persons reports that the price of a generic prescription averages 30% to 50% below that of a brand name drug. Approximately 80% of prescription drug products are now available in generic form, and this includes many of the most widely prescribed in the United States. Consumers save hundreds of millions of dollars annually by using generic drugs, and all 50 states now have some form of generic substitution laws to encourage the use of generic drugs.

Long-term estimates of health care costs for this nation are predicated on the continued availability of safe and effective generic drugs.

Part Two: The Problem--Illegal Gratuities and Fraud

On April 27, 1989, Representative John Dingell, Chairman of the House Subcommittee on Oversight and Investigations, and the U.S. Attorney for Baltimore announced criminal charges against representatives of the generic drug industry for offering illegal gratuities to a federal employee and against one employee of the U.S. Food and Drug Administration for accepting the gratuities. They also announced that they had evidence that another FDA employee had been linked to illegal gratuities.

In late June, Vitarine Pharmaceuticals, Inc., a generic drug firm located in Springfield Garden, New York, was discovered by FDA to have submitted to FDA data that it fraudulently represented to be data gathered on its generic copy of a drug.

These revelations of illegal gratuities and outright fraud stood as stark evidence that the review process for generic drugs, which had been based in part on an honor system that relied on the integrity of generic drug firms, had been severely compromised by a few of those firms.

FDA was as outraged and morally affronted by these charges as the American people were. Furthermore, FDA was distressed that

ultimately three of its employees, who have since resigned, compromised the public trust by accepting illegal gratuities.

With the breach of the integrity of this system came the fundamental question: can the millions of Americans who take generic drugs every day continue to rely on them? To answer these questions, Secretary Sullivan announced an action plan and Commissioner Young formulated an implementation plan on August 18. This interim report issued 89 days after the announcement of the plan. It focuses on how the FDA tackled that question head on, and it provides the basis of the FDA's recommendation that American consumers should continue to have confidence in generic drugs currently on the market. Finally, it outlines what the Government has already done or has begun to do to prevent a recurrence of the problem.

Part Three: A Primer on Generic Drugs

The discovery of new pharmaceuticals is accomplished principally by the research intense pharmaceutical companies. These companies invest an average of \$100 million per drug developed. Each prescription drug has two names: the chemical name and the brand name. Once the patent on the original brand name drug has expired, other companies may seek FDA's approval to manufacture and sell a "copy" of the brand name drug. The new

competitor drug, which has the same active ingredients and the same chemical name as the original drug, is a generic drug.

Companies that develop innovative new drugs must submit to the FDA proof in support of the drug's safety and effectiveness. Generic drug manufacturers do not have to submit safety and effectiveness data in their abbreviated applications, because their product should be a duplicate of--or identical in the essential aspects of--the original or brand name product.

To be approved by the FDA for marketing, generic drugs must work in the same way in humans as brand name drugs that the FDA has already approved as safe and effective. This provides assurance that the generic drugs are therapeutically equivalent to their brand name counterparts. Under the law, each manufacturer of a generic drug must show that its product is bioequivalent--that the active ingredient is absorbed into the human body at about the same rate and to the same extent as the brand name product. In certain instances, it is difficult to manufacture a generic copy and demonstrate its bioequivalence.

In FDA's review of applications to market generic drugs, therefore, the point at issue is the manufacturer's ability to make a version of the original drug, with the same active ingredient, that acts in the body in a similar way.

Part Four: Can Americans Continue to Rely on Generic Drugs?

Since the reports of illegal gratuities, fraud and other problems became known last spring, consumers and health professionals around the country have frequently asked FDA whether generic drugs are safe, and whether they work. FDA has emphasized, and other outside investigators have confirmed, that on the basis of the considerable evidence now at hand, no serious problems with the safety of generic drugs have been found to date.

This conclusion is based on FDA laboratory testing of more than 2,500 samples of generic drugs, and intensive FDA inspection of 20 of the largest generic drug firms and contract laboratories that perform research testing on generic drugs. The majority of this work is now complete.

FDA's inspections did reveal batch-to-batch manufacturing problems for some generic firms, but these problems were no more severe than those routinely found in brand-name drug firms and generic companies alike. There have also been reports that two epileptics died after being switched from the branded to a generic version of carbamazepine. The FDA has investigated those cases and has found no causal link between the generic drug and the two deaths.

Whenever the FDA uncovered fraud or where possible safety or

effectiveness problems arose (as in the case of carbamazepine), swift action was taken to obtain product recalls and the withdrawal of approvals for certain generic drugs.

FDA Laboratory Testing

FDA's findings about the safety of generic drugs is based in part on its own laboratory testing. On August 13, 1989, at the request of Commissioner Young, FDA began collecting samples of the thirty most prescribed generic drugs, representing about three-fourths of generic new prescriptions, along with their brand-name counterparts. As of November 3, 1989, the Agency had collected and analyzed over 2,500 samples representing the top 30 prescribed generic drugs. (The drugs are listed in an appendix to this report.)

FDA laboratories analyzed these top-selling generic drugs for conformity with standards established by the United States Pharmacopoeia (USP) or the FDA (i.e., potency, dissolution content uniformity, product identification, and purity). These standards provide a method of determining the conformity of one product to another.

Of the more than 2,500 samples collected, only approximately one percent were out of compliance. These are significant results, for they mean that nearly 99% of the drugs sampled comply with USP

and/or FDA standards. This ratio is consistent with historical rates for brand-name and generic drug products. Thus, it is reassuring that such a large proportion of generic drugs that are the most frequently prescribed were found to have a low deficiency rate, one that is typical of the drug industry as a whole.

During the past several months, FDA has also been evaluating samples of specific generic drugs that generic drug firms submitted to contract laboratories for bioequivalence testing. FDA's re-testing became necessary because of evidence that brand name products had been switched for the generic versions in submissions for bioequivalence testing.

In this portion of the investigation, two FDA laboratories are in the process of analyzing more than 1,500 drug samples originally presented by generic drug firms for bioequivalence testing. The FDA has given priority to drug samples submitted by the firms involved in corrupt activities, fraud, or sub-standard manufacturing practices. These analyses are extremely complex and time-consuming. Irregularities must be cross-checked between plant records and data in the firm's application. Although this process is not yet complete, results to date are reassuring. FDA has found only one additional instance of substitution thus far.

Further, FDA has initiated a program to analyze generic drug

products that have a narrow therapeutic range or that are hard to duplicate. Drugs that have a narrow therapeutic range--such as certain drugs to treat epilepsy--or ones that are difficult to manufacture may pose a greater public health risk if safety or effectiveness is compromised. Recommended dose levels for drugs are usually conservative, and so for most drugs minor variations in potency are acceptable. In fact, all prescription drugs--whether brand-name or generic--are permitted to vary within a small range of their approved potency and still be considered appropriate therapeutically. But certain drugs are difficult to manufacture or have a narrow therapeutic range, and for these additional scrutiny is in order.

FDA Inspections

Shortly after the revelations about illegal gratuities became known to FDA this spring, FDA began in-depth inspections of 11 generic firms suspected of possible wrongdoing. (Subsequently, five more firms were inspected "for cause.") As a result of these inspections, FDA uncovered serious problems with nine of the 11 firms. These problems included fraudulent ANDA submissions, "cutting corners" during the manufacturing process, and other manufacturing deficiencies.

To determine whether problems found in the 11 suspect firms were more widespread in the generic drug industry, FDA initiated

inspections of a cross section of the industry. Twenty firms were chosen, many of which were the largest firms in the industry.

The agency has not yet completed its evaluation of the results of these inspections. The most serious problem discovered to date in the 20-firm inspection program--and one that fortunately occurs seldom in the drug industry--involved one firm that had falsified batch records for a number of products. The firm recalled the multiple strengths of eleven drugs and stopped distribution of its other generic products.

These inspections also revealed a number of deficiencies in the manufacturing process. Because the manufacture of pharmaceutical products is a complex procedure, deviations in the process are not unusual and do not result from fraudulent behavior. It should be emphasized that such deficiencies nearly always have little or no effect on the safety and efficacy of drug products, and that they do not ultimately translate into the production of defective drugs. Such problems are routinely corrected, either by drug firms themselves or at the request of FDA after an inspection.

Regrettable as the incidents of fraud and illegal gratuities are, it is important to note that neither kind of misconduct has resulted in the compromise of safety of the generic drug supply. In other words, there is no evidence that criminal actions

apparently intended to win FDA's approval of generic products sooner have caused an unsafe product to be approved or sold.

FDA's investigation of fraud in the generic drug industry focused on generic drug samples submitted to independent contract laboratories for bioequivalence testing. In the approval process, the generic drug firm must show that the drug is identical and also gets into the blood stream at the same rate as the name-brand drug. Thus the analysis of the rate of absorption and entry into the blood stream in healthy volunteers would show whether the generic drug is the same functionally as the brand name.

To summarize: FDA's laboratory tests of the "top-30" drugs and the contract laboratory samples provide good assurances about generic drugs. But the findings from FDA's inspections of generic firms--while still incomplete--have raised questions. The FDA shall remain vigilant in its oversight of the generic drug industry, and shall continue to follow through on the inspectional findings.

On the basis of various factors discussed above, FDA has concluded that, while certain questions remain to be answered, consumers should continue to use generic drugs currently on the market.

Part Five: Preventive Measures

Most of the FDA's short-term work on generic drugs has focused on the sampling, analyses, and inspections just described. For the long-term, FDA and its parent Department of Health and Human Services have developed an ambitious action plan designed to prevent similar instances of fraud and illegal gratuities in the future.

As announced by the Secretary of Health and Human Services, Louis W. Sullivan, M.D., and Frank E. Young, M.D., Ph.D., Commissioner of Food and Drugs, on August 18, 1989, this plan comprises six elements.

First, intensified analyses of generic drugs and firms. In addition to the actions already described, FDA will maintain a higher "baseline" of surveillance over the generic drug industry. If problems are discovered, FDA will take vigorous enforcement actions. As always, safety concerns will receive paramount attention.

Specifically, FDA plans to expand its surveillance of generic drug firms by adding more personnel to inspect drug development from the manufacture of the first samples through to the market place. In addition, FDA will conduct surprise spot checks of the

market to determine bioequivalency.

Second, a reorganized and strengthened drug review program.

This includes a newly-created office of generic drugs, new leadership for the office, increased staffing and space, creation of a technical scientific advisory committee, and implementation of the recommendations provided in the Inspector General's audit of the generic drugs program initiated by Commissioner Young.

Third, the establishment of an independent ombudsman reporting directly to the FDA Commissioner. The ombudsman will resolve disputes between the FDA and companies that feel disadvantaged, and will act on all complaints concerning potential safety, effectiveness, or fairness problems associated with all FDA-regulated products, including generic drugs.

Fourth, closer and more effective coordination on criminal investigations between the FDA and the Inspector General of the Department of Health and Human Services. The Office of Inspector General will support FDA in criminal investigations, at the FDA's request. The FDA will work closely with the Inspector General when charges of wrongdoing involving FDA employees become known.

Fifth, new legislation to strengthen and clarify the Secretary's authority to act promptly against any improper activity

in connection with drug approval applications. This legislation will provide flexible means by which the Secretary and the FDA can protect the public health, punish wrongdoers, and assure continuing public confidence in the nation's supply of drugs.

Sixth. alternative methods of financing to supplement the corrective actions taken thus far. FDA needs additional resources to support increased surveillance of the generic drug industry. The FDA will cooperate with the Administration and Congress to determine how to meet these resource needs. In the absence of additional resources, increased inspections and enhancements in the quality of the review process will not occur.

Endnote

The generic drug industry, which has produced a growing number of useful and more affordable drugs (especially since 1984), has suffered a serious setback. Two types of devious behavior--fraud and illegal gratuities--were used by a few generic drug firms in attempts to gain a competitive advantage.

The long-term survival of this industry depends heavily on the ability of the industry, the FDA and the Congress to turn adversity into opportunity. To do this will require the highest integrity by the manufacturers and by the FDA as it regulates this industry.

The most important questions, of course, and the one most frequently asked of FDA, are these: "Are generic drugs safe?" and "Do these products work?" On the safety side of the equation, FDA has found no evidence to date indicating that generic medications now in use pose a serious public health threat. The medical community has utilized generic drug products effectively in its continued fight against disease and suffering. Given the appropriate level of resources, the FDA will enhance its work of monitoring and evaluating the generic industry. Each of the actions outlined is designed to continue to maintain that level of assurance. FDA will remain aggressive in its regulatory oversight primarily by increased inspection and aggressive enforcement action. The end result of these actions will ensure that generic drugs are equivalent and thus work as their brand name counterparts.

For now, however, consumers should continue to use generic drugs. If the generic medications they are taking are working, they should continue with them. If consumers have questions or concerns about their generic prescriptions, they should consult their physicians or pharmacists. Consumers can be assured that if generic drugs are found to be unsafe or ineffective, FDA will act vigorously and appropriately.

FDA is confident that all of the actions it is taking will

strengthen the generic drug industry. These actions will also better protect FDA employees from possible future offers from any would-be industry "crooks," who will now think twice before attempting to gain favored treatment or circumvent the regulatory process.

The three former FDA employees that betrayed their public trust by accepting illegal gratuities have left a blemish on the FDA, an agency with a proud 83-year tradition of consumer protection. But these three malefactors should not--they cannot--be viewed as emblematic of the remaining 7,500 FDA employees who are pledged to uphold that tradition.

Indeed, it remains the responsibility of the generic drug industry to regain its credibility by putting its own house in order while FDA upgrades and improves its regulatory processes. Reliability and honesty must be the watchword of both. The new system will provide an even greater guarantee than in the past that generic drugs are safe and effective, and the FDA shall not rest until the various tasks are completed and the changes have been carried out.

TOP 30 PRESCRIBED DRUGS
GENERIC DRUG SURVEY

1. ACETAMINOPHEN/CODEINE
2. ALLOPURINOL
3. AMITRIPTYLINE HCL
4. AMOXICILLIN
5. AMPICILLIN
6. CEPHALEXIN
7. DIAZEPAM
8. DIPYRIDAMOLE
9. DOXYCYCLINE
10. ERYTHROMYCIN
11. ERYTHROMYCIN STEARATE
12. FERROUS SULFATE
13. FUROSEMIDE
14. HYDROCHLOROTHIAZIDE
15. HYDROCORTISONE
16. IBUPROFEN
17. IMIPRAMINE HCL
18. LORAZEPAM
19. MECLIZINE HCL
20. METRONIDAZOLE
21. NITROGLYCERIN
22. NYSTATIN
23. PENICILLIN V POT.
24. PHENOBARBITAL
25. PREDNISONE
26. PROPOXYPHENE NAPSYLATE/ACETAMINOPHEN
27. TETRACYCLINE
28. THYROID
29. TRIAMCINOLONE
30. TRIMETHOPRIM/SULFAMETHOXAZOLE

Food and Drug Administration
Rockville MD 20857

13 1989

Dear Consumer:

As a member of the Generic Drug Network, you may use the enclosed material to continue to respond to the concerns raised by your constituencies. As you know, the Food and Drug Administration (FDA) has undertaken many steps to assure the quality of generic drug products, and is moving as swiftly as possible. If safety or efficacy problems are discovered, FDA will act to remove those products from the market immediately.

FDA has found that data may have been misrepresented in three drug applications submitted by Quantum Pharmics (10/20/89 Talk Paper). The parent company, American Home Products, agreed to recall these products and several others because of misrepresented data. In all, multiple strengths of 12 drugs were recalled. However, there is no known safety problem with the products. In addition, production and distribution of all 21 Quantum generic drug products have been suspended.

We recently notified you that Bolar had begun a voluntary recall of nitrofurantoin macrocrystals from its distributors and wholesalers. On October 25, after FDA presented additional sample evidence that the brand name product had been substituted for the generic in bioequivalency tests, Bolar extended the recall to pharmacies and other retail outlets. FDA has begun proceedings to withdraw the application for this product since the Agency can no longer state that the Bolar product is interchangeable with the brand name drug (10/27/89 Talk Paper).

On November 17 FDA Commissioner Frank Young will appear before the House Subcommittee on Oversight and Investigations. In his statement, Dr. Young will summarize the current status and findings of FDA's comprehensive review of the generic drug industry. The Agency plans to release an interim report on generic drugs, a copy of which will be provided to you at that time.

We hope you find this information useful in responding to the concerns of your constituents about generic drugs.

Sincerely yours,

Alexander Grant

Alexander Grant
Associate Commissioner
for Consumer Affairs

Enclosures

TALK PAPER

FOOD AND DRUG ADMINISTRATION
U.S. Department of Health and Human Services
Public Health Service 3600 Fishers Lane Rockville, Maryland 20857

Talk Papers are prepared by the Press Office to guide FDA personnel in responding with consistency and accuracy to questions from the public on subjects of current interest. Talk Papers are subject to change as more information becomes available. Talk Papers are not intended for general distribution outside FDA, but all information in them is public, and full texts are releasable upon request.

T89-67
Oct. 20, 1989

Bill Grigg
(301) 443-3285

QUANTUM DRUGS RECALLED

(Updates T89-60 Generics Investigations, Oct. 3, 1989)

When FDA found indications that data may have been misrepresented in three drug applications that had been submitted by Quantum Pharms of Amityville, N.Y., the company's new owner, American Home Products Corp. of New York, N.Y., agreed to recall the products.

FDA requested the recall of Quantum's minoxidil tablets, chlorazepate dipotassium tablets and meclofenamate sodium capsules because the size of the production run submitted for testing to gain FDA approval was in each case misrepresented as much larger than it actually was. Also, in the case of the meclofenamate sodium capsules, it was uncertain whether the product formula tested is the same that was approved and is being marketed.

American Home Products has agreed to recall four other products — trazadone, doxepin, diazepam and lorazepam — because of concerns about data submitted to the original applications. These Class II recalls are the result of misrepresented data and similar problems in the Quantum applications resulting in a lack of assurance of bioequivalence. No safety problem with the products is known.

American Home Products has told FDA it was suspending production and distribution of all 21 of Quantum's generic drug products pending the completion of an exhaustive internal audit.

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TALK PAPER

FOOD AND DRUG ADMINISTRATION
U.S. Department of Health and Human Services
Public Health Service 5600 Fishers Lane Rockville, Maryland 2

FDA Talk Papers are prepared by the Press Office to guide FDA personnel in responding with consistency and accuracy to questions from the public on subjects of current interest. Talk Papers are subject to change as more information becomes available. Talk Papers are not intended for general distribution outside FDA, but all information in them is public, and full texts are releasable upon request.

T89-68
Oct. 27, 1989

Mike Shaffer
(301) 443-3285

BOLAR RECALLS NITROFURANTOIN

(Updates T89-60 Generics Investigations, Oct. 3, 1989)

Bolar Pharmaceuticals of Copiague, N.Y., has agreed to recall its generic nitrofurantoin macrocrystalline antibiotic capsules to the retail level. The firm had on Oct. 6 said it was ceasing distribution and recalling the product only from its direct accounts -- such as distributors and wholesalers. The new action takes the recall through the distribution chain to the pharmacy level.

The product is a generic version of the Norwich Eaton product called Macrochantin, an antibiotic used primarily to treat urinary tract infections. The 50 mg. and 100 mg. capsules are being recalled because of evidence that Bolar substituted the brand name product in place of its own for bioequivalence testing. As a result, although no health problems are known to be associated with the product, FDA cannot assure that it is equivalent to its brand name counterpart.

FDA had asked Bolar to recall the drug to the retail level earlier but the firm suggested that the problem did not justify such a recall. On Oct. 25, after FDA presented additional sample evidence from a second laboratory, Bio-research Laboratories Ltd. of Quebec, to support its view that the brand name product and the generic were switched for testing, the firm agreed to extend the recall to pharmacies and other retail outlets.

-MORE-

Page 2

On Oct. 13, FDA informed Bolar that it is proceeding to withdraw the firm's Abbreviated New Drug Application for this product, which would mean the company could not make the product in the future. In addition, FDA has downgraded the product's therapeutic evaluation rating from "AB" (equivalent) to "BX" (presumed inequivalent). This change alerts pharmacists that FDA can no longer state that the Bolar product is interchangeable with the original Norwich Eaton product. Although other nitrofurantoin products are available, the Bolar product was the only generic available as macrocrystalline capsules.

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DEPARTMENT OF HEALTH & HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

Food and Drug Administration
Rockville MD 20857

JAN 23 1990

Dear Consumer:

An article titled, "Ensuring the Safety of Generic Drugs," by Dr. Frank Young appeared in the most recent edition of FDA Consumer. The article offers an update on FDA's 6-point plan of action designed to ensure an adequate supply of safe and effective generic drugs.

Enclosed is a copy of the article which you may disseminate to your constituents.

FDA is recommending that consumers of generic drugs continue to take their medication unless advised differently by their doctors or pharmacists.

Sincerely yours,

Alexander Grant
Associate Commissioner
for Consumer Affairs

Enclosure



Ensuring the Safety of Generic Drugs

by Frank E. Young, M.D., Ph.D.
Commissioner of Food and Drugs

By now, much of the nation has heard at least something about the Food and Drug Administration's investigation of the generic drug industry. The investigation has not only gripped the agency over the past several months, but also has had broad impact on an industry whose products represent about one-third of the prescriptions filled in the United States each year.

The generic drugs saga that unfolded over the summer has been rather complicated. At times, it has been difficult, even for me, to separate the wheat from the chaff in all of the various accounts of what has happened. In this issue of *FDA Consumer*, I would like to describe what's happened with respect to generic drugs, and what FDA has done to respond.

FDA takes its responsibility of ensuring the quality of all drugs—generic and brand-name—very seriously. This is our ongoing mission, and we shall always act promptly to remove from the market any drug that is found to fall short of our high standards.

The generic drug saga has underscored a point seen so often in life: that the poor behavior of a few tends to obscure the good done by the many. This is not to suggest that we do not have serious concerns about the conduct of a small handful of generic drug companies and three of our own former FDA employees. The entire agency, myself included, feels a deep sense of hurt and anger at the conduct of three of our own. Clearly, there was a problem, and a remedy was needed.

The problem, as it has unfolded, has at least three distinct parts. Let me explain:

It was discovered that officials of some generic drug firms offered illegal gratuities to FDA employees in our generic drug program. Regrettably, three FDA employees—now former employees—accepted the offers. These employees represent a tiny fraction of the 7,500 dedicated public servants who make up the FDA and of the 80 or so persons who work in the office that reviews generic drugs. I'm not trying to diminish the crimes, but I do want to keep in the proper perspective the work of the vast majority of FDA employees.

The second, and perhaps even more fundamental, part of the problem was the discovery that several generic drug firms had submitted false data in their applications to FDA for approval

to sell new generic drugs. For example, one generic company admitted to submitting the brand-name maker's drug as its own in an effort to win swift approval of its generic copy.

Truthful and accurate information submitted by companies that manufacture drugs is crucial to FDA's continuing ability to ensure that their products are properly tested and manufactured.

Finally, FDA has also uncovered evidence that some generic drug firms have violated the good manufacturing practice regulations that govern overall production procedures and techniques that help guarantee the safety and effectiveness of drug products.

These revelations required the agency to act swiftly and conclusively to ensure that what was on the market was safe and effective for consumers of generic drugs. And, on Aug. 18, 1989, Health and Human Services' Secretary Louis Sullivan announced a comprehensive plan to accomplish this important objective. As part of that plan, with the help and support of the secretary's office, we are preparing new proposals for the Congress to seek to make certain that these problems do not occur again.

First and foremost, we needed to ensure that generic drugs are safe. Last April, when the allegations of gratuities first came to light, FDA launched "for cause" inspections of 11 generic drug firms. That number eventually grew to 13 firms after some irregularities in two other companies were reported by FDA investigators.

When we discovered that some companies had provided false data to FDA in the application process, we took a second major step—a comprehensive sampling and analysis of the 30 most-prescribed generic drugs. Our FDA labs across the country worked exceptionally hard to complete this huge task. I was able to visit several of the labs during this time and see for myself the painstaking work our laboratory staff were doing. Generic drugs, as well as the brand-name counterparts, were tested to make sure that each had the proper qualities of potency, dissolution and composition. The results of these tests showed no significant difference in the quality of these generics compared to the brand-name products.

These exhaustive laboratory tests have enabled FDA to pro-



protect consumers from generic drugs that do not conform to current standards. It is our belief that this process allows us to solve the issue at hand—ensuring the quality of generic drugs.

In addition to testing the top 30 generic drugs, we launched a second wave of inspections involving 20 additional drug companies that manufacture generics. These inspections, which also include some brand-name makers who make generic drugs as well, were not prompted by any wrongdoing; rather, the firms were selected because they market a broad array of generics.

It is important to note that we have not received any unusual reports of quality problems with the use of these drugs. We took these actions because we felt they were warranted, given the serious allegations of misconduct that came to light earlier this year.

The plan of action put forward with the secretary's help will, we hope, prevent problems such as the ones I've outlined from recurring.

First, in addition to the plan's call for expanded field inspections, we are reorganizing and strengthening the generic drug review procedures. We are recruiting proven managers to oversee a reorganized and enhanced Office of Generic Drugs, and are establishing a quality control function to make sure that our reviews of new generic drugs are fair and based on sound science. This new office will have increased staff and will report to the director of the Center for Drug Evaluation and Research, Dr. Carl Peck.

Second, we are creating a technical scientific advisory committee on generic drugs. Drawing on the approach successfully used in other FDA product review areas, this committee will provide expert outside counsel on problematic and complex scientific issues.

Additionally, we are establishing an independent ombudsman who will report directly to me. This ombudsman will investigate and seek to resolve disputes between FDA and companies that feel disadvantaged, and pursue complaints that involve potential problems of safety, effectiveness or fairness in-

volving approval of generic drugs as well as other FDA-regulated products.

Fourth, we will work more closely with the inspector general of HHS. As in the past, the inspector general will support FDA in criminal investigations when FDA requests this assistance. We will also continue to work closely with the inspector general should any matters arise that involve charges of wrongdoing by FDA employees.

Fifth, as noted earlier, we are working with HHS in developing legislation to strengthen the department's authority to act promptly against criminal activity in connection with the drug evaluation process.

Finally, we are continuing to seek ways to finance these activities and others carried out by the agency to protect and serve the American consumer.

The actions of a few individuals have seriously eroded the honor system upon which much of the generic drug review process has been based. Now, we will strengthen that system with a "trust, but verify" approach.

Throughout the generic drugs saga, I've been frequently asked what I would advise a patient who was taking generic prescription drugs. My advice is simple: If the medicine is working, continue to take it. If you are given a new prescription and want to take the generic version of the drug, consult your physician or pharmacist. They will have the latest information on any problems that may exist with respect to prescription drugs, both brand-name and generic.

I've always been an advocate of greater communication between patient and physician. The silver lining to the cloud of the generics investigation is that it may have encouraged patients to take a closer look at the medicines they were taking and to discuss them with their doctors.

I believe that, ultimately, the combination of FDA's continued efforts to ensure safety and effectiveness and better communication between patients and physicians will mean that the nation's confidence in the prescription medicine supply will be stronger. That's a pill we all can swallow. ■



Food and Drug Administration
Rockville MD 20857

FEB 2 1990

Dear Consumer:

This letter is to provide you with the latest information regarding the Bolar Pharmaceutical Company's generic drug Dyazide (triamterene 50 mg./hydrochlorothiazide 25 mg.) and generic drug Dilantin (phenytoin sodium 100 mg. extended release capsules). Bolar's generic Dyazide is used to treat hypertension and its generic Dilantin is used to prevent seizures.

The Bolar Pharmaceutical Company has voluntarily ceased production and distribution of generic Dyazide and Dilantin and has begun a recall of these products. The reason for the recall is that bioequivalence cannot be assured in view of the questions raised by the Food and Drug Administration (FDA) concerning the documentation supporting the approval of Bolar's Abbreviated New Drug Application. The FDA is moving rapidly to revoke Bolar's approved Abbreviated New Drug Application for its generic version of Dyazide.

The FDA urges consumers not to abruptly stop taking either medication.

The FDA advises that consumers may take generic Dyazide until their prescription runs out but should consult with their physician as soon as possible. Consumers who take Bolar's generic Dilantin should consult with their physicians as soon as possible.

We hope this information is helpful to your constituencies and urge consumers of these drugs to consult with their physician.

Sincerely yours,

Alexander Grant
Associate Commissioner
for Consumer Affairs

Enclosure

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BLR COUNSEL

P.03

**BOLAR PHARMACEUTICAL CO., INC.**

80 Ralph Avenue, P.O. Box 20, Copeague, New York 11796-0020
(516) 642-8365, FAX (516) 642-6620

January 31, 1990

To Our Customers:

RE: URGENT DRUG RECALL - TRIAMTERENE 50 mg./HYDROCHLOROTHIAZIDE
25 mg. CAPSULES
PHENYTOIN SODIUM 100 mg. EXTENDED
RELEASE CAPSULES

Bolar is voluntarily recalling all lots of its products Triamterene 50 mg. / Hydrochlorothiazide 25 mg. capsules and Phenytoin Sodium 100 mg. Extended Release capsules.

The products are being recalled because their bio-equivalence cannot be assured in view of the questions raised concerning the documentation supporting the approval of their Abbreviated New Drug Applications.

You are hereby requested to immediately cease distribution of both Triamterene 50 mg. / Hydrochlorothiazide 25 mg. capsules and Phenytoin Sodium 100 mg. Extended Release capsules. Remove the products from your shelves and return them promptly to Bolar, freight prepaid. Your account will be credited accordingly for product and freight. We are requesting and you are authorized to extend this recall to your customers.

Enclosed are two (2) post cards that we ask you to fill out and return to us immediately, informing us of the amounts of product involved under your direct control that we may expect to receive under this recall. If you do not have any product, please indicate "NONE".

We thank you for your immediate attention to this situation. If you have any questions please call your sales representative.

Sincerely,

Robert Shulman, President

ENCL:

RS/pf

**BOLAR PHARMACEUTICAL CO., INC.**

20 Ralph Avenue, P.O. Box 80, Coney Island, New York 11738-0080
(516) 842-8383, FAX (516) 842-8830

TO: Editor, Business News
FROM: BOLAR PHARMACEUTICAL CO., INC.
Patricia Shukri
DATE: January 31, 1989

Bolar Pharmaceutical Co., Inc. advised the FDA yesterday that it ceased production and distribution of Triamterene 50 mg. / Hydrochlorothiazide 25 mg. capsules [the Company's generic version of Dyaside (R)] and has begun a voluntary recall of that product and of Phenytoin Sodium 100 mg. Extended Release capsules (Phenytoin). Bolar had ceased distribution of Phenytoin in December, 1988.

These actions have been taken because the products' bio-equivalence cannot be assured in light of serious questions concerning the accuracy and reliability of the documentation supporting the approval of the Abbreviated New Drug Applications for these products.

Bolar is currently engaged in conducting new bio-equivalence studies for both products and intends to submit the results of these studies to the FDA when they are completed. The results of these studies will not be available for at least 3 months. No assurance can be given that these studies, when completed, will establish bio-equivalency or, even if they establish bio-equivalency, that the products will be re-approved for sale by the FDA. Furthermore, even if the products should be re-approved



BOLAR PHARMACEUTICAL CO., INC.

Page 2

by the FDA, no assurance can be given that there will be a market for these products.

Bolar estimates its net sales for 1989 to be approximately \$133 million on an unaudited basis prior to adjustment for this recall; sales of Bolar's generic version of Dyaside (R) accounted for approximately 38% of 1989's net sales and sales of Phenytoin accounted for approximately 2% of 1989's net sales, both on an unaudited basis. It is estimated that these 2 products would have accounted for approximately 52% of the Company's income before taxes and extraordinary items for 1989, with Bolar's generic version of Dyaside (R) accounting for substantially all of this percentage. Bolar previously announced a recall of Nitrofurantoin Macrocrystals 50 mg. and 100 mg. capsules which, together, accounted for an additional 7% of 1989's net sales and an additional 1% of income before taxes and extraordinary items for 1989.

Bolar cannot, at this time, anticipate when or whether it will be able to resume sales of its generic version of Dyaside (R). The absence of sales of Bolar's generic version of Dyaside (R) will have a material adverse effect on earnings.

The Company's internal investigation is continuing. Bolar will continue to take appropriate action).

FDA Statement on Bolar's generic Dyazide and generic Dilantin Recall

For both of these products, patients should consult with their physicians and are urged not to stop taking either medication abruptly.

Bolar's generic Dyazide (triamterene/hydrochlorothiazide) is used to treat hypertension. FDA advises that patients may continue taking this product until their prescription runs out and they can arrange with their physician to take another medication.

Bolar's generic Dilantin (phenytoin) is used to prevent seizures. FDA advises that patients taking this drug should consult with their physicians in the next few days about alternative medication.

The Food and Drug Administration still intends to revoke Bolar's approved Abbreviated New Drug Application (ANDA) for its generic of Dyazide. That process is moving forward rapidly.

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Dear Consumer Letters

Generic Drug Network

List of Attachments

Date of Letter

October 25, 1989

November 13, 1989

November 20, 1989

January 9, 1990

January 23, 1990

February 2, 1990

Attachments

Dr. Young's Remarks 9/13/89

Talk Paper Generics InvestigationsBolar voluntary recall of
nitrofurantoin (Bolar
Statement and FDA Statement)

Federal Register - Withdraw Vitrine

Talk Paper Quantum Drug Recall

Interim Report on Generic Drugs

List of Generic Drug Product
Suspension, Recall and Withdrawal
Actions (week ending 12/29/89)Dr. Young's article, "Ensuring the
Safety of Generic Drugs" (FDA
Consumer, Dec.89/Jan.90)FDA Statement on Bolar's generic
Dyazide and generic Dilantin Recall



DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Director

Food and Drug Administration
Rockville, MD 20857

OCT 25 1989

Dear

On behalf of the Commissioner of Food and Drugs, I would like to thank you for your participation in the September 13 meeting of the Leadership Council of Aging Organizations. Dr. Young appreciated the opportunity to discuss the generic drug situation with you, to respond to the concerns you raised on behalf of your constituencies, and to explore ways that we can work with you to continue to respond to the concerns of elderly consumers on generic drugs.

As Dr. Young stated at the September 13 meeting, the Agency takes its consumer protection responsibilities very seriously and is committed to ensuring consumers a safe and effective generic drug market. This commitment is embodied in an action plan that was developed by Dr. Louis Sullivan, Secretary of the Department of Health and Human Services and the Agency. A more detailed description of this plan is provided in the enclosed copy of the remarks that Dr. Young made at the meeting.

The FDA plan of action provides a multi-faceted approach for ensuring a safe and effective generic drug supply. This approach involves laboratory analysis of market and premarket testing samples, manufacturer inspections and needed regulatory actions, management and administrative actions, legal and legislative actions, and consumer information and education activities. In combination, each of these areas will help to provide consumers with a renewed confidence in the safety and effectiveness of generic drugs.

Under this plan, a number of significant actions have occurred that we would like to share with you so that you can inform your membership and constituencies. Enclosed is a FDA Talk Paper (October 3, 1989) which describes the efforts undertaken by the Agency to resolve all uncertainties associated with the production of generic drugs and the manner in which they are approved. As a result of its laboratory analysis and inspection activities, the Agency published a notice in the October 3 Federal Register

Page: 2

proposing to withdraw approval of certain drug applications held by Vitarine Pharmaceuticals, Inc. because the applications contain untrue statements of material fact and that the drugs covered by these applications lack substantial evidence of effectiveness. This notice offers the public the opportunity to submit comments on the notice; a copy of this notice is enclosed.

Most recently, FDA met on October 6 with Bolar Pharmaceutical Co., Inc. to present evidence FDA has uncovered indicating that the company substituted the innovator drug for its own during bioequivalency testing of the generic drug nitrofurantoin. At this meeting, FDA asked Bolar to recall its generic version of Macrochantin, which is the brand-name of this drug, used to treat mild urinary tract infections. On October 8, Bolar announced that it has begun a voluntary recall of nitrofurantoin macrocrystals 50mg and 100mg capsules. Enclosed for your information are the FDA Statement on Bolar Pharmaceutical Co., Inc. (October 6, 1989) and the Recall Announcement issued by Bolar Pharmaceutical Co., Inc.

Consumers who are currently taking the generic drugs involved in these actions should not stop taking the medicine until they have consulted with their physician. If consumers would like more information, they can contact their local FDA office (the number is listed in the phone book) or call the FDA Office of Consumer Affairs on 301/443-3170.

I hope you find this information to be useful and I look forward to working closely with you to establish an effective information exchange for responding to the concerns that elderly consumers have about generic drugs.

Sincerely yours,



Alexander Grant
Associate Commissioner
for Consumer Affairs

Enclosures

Mr. HADDAD. There was one sentence I left out of my testimony that I think is appropriate. It might be helpful here.

I said, "I'm not trying to condone the illegal, unethical, abhorrent behavior of the generic companies who violated and abused the public trust. They have and will pay their penalties under law and in the marketplace," because they're not buying from these companies out there now that are going to be on the list you'll see.

I doubt if any of the guilty companies will survive in their current form.

Ms. LLOYD. That leads up to a question that I had for you. Are these companies that you mentioned, are they still members of your association?

Mr. HADDAD. No. We've—

Ms. LLOYD. Removed them?

Mr. HADDAD.[continuing] removed the companies. They've all been asked to leave the association.

Ms. LLOYD. Bolar, Parr, and Quad?

Mr. HADDAD. Bolar, Parr, and Quad are no longer members. Parr, as you know, is undergoing a reorganization. Bolar's situation is very recent.

Ms. LLOYD. In your statement you said—and it was a very fine statement—that honest generic drug companies are now being severely damaged, but then the business in generic drugs has increased 13 percent.

Mr. HADDAD. Well, individual companies—

Ms. LLOYD. Are the processes coming along pretty well?

Mr. HADDAD. Well, there are two things that happened. We had the law change and the industry expanded. A lot of companies expanded in anticipation of a flow rate of new products coming off market. So they're sitting there with plans and unused capacity for products that they were looking to make.

Some very innocent companies are having trouble. I know FDA is aware of it.

For example, if you want to move products from plant A to plant B, you go through a relatively shorter process than you do for an ANDA. A lot of people are caught between one place and another. They're having that kind of problem.

Some of the business has gone back to the brand-name companies. Brand-name companies make generics.

Ms. LLOYD. Mr. James?

Mr. JAMES. Yes, thank you.

What does it accomplish if you prevent a company from dealing with drugs when all you do is change the name of it or reorganize and transfer it to another corporate setup?

Mr. HADDAD. I was a journalist in Germany after World War II and I saw the emergence of a lot of these companies under new names with the same ownership. I wrote some very strong stories about that, and I have some very strong personal feelings about it.

But, you're dealing with law and corporate entities. What if the Lily situation which—

Mr. JAMES. Perhaps the question ought to be addressed to the attorney in this case.

When these companies were prosecuted, the ones that have been prosecuted—and I take it there have been—what were the fines paid in the instances, the major fines paid, if any?

Mr. ADAMS. If you'll give me just a moment, I have some documents. I can give us those figures.

Mr. JAMES. Yes. And I would like to know the individuals and what they paid, what their sentences were in general, what the plea bargaining was, what level they were in the company, if you have that information—to just see how severe the Government did react to that scenario.

While he's looking for that, here's another question for Dr. Peck: in your testimony, which I think you skipped over this paragraph, "We believe it is appropriate that the cost of maintaining this confidence should be borne by that industry. We are, therefore, requesting that FDA's generic drug budget be financed through user fees." Is that part of your testimony?

Dr. PECK. Yes, that's in the submitted testimony.

Mr. JAMES. Yes, I note that. But I think you skipped over that paragraph for the sake of brevity.

But, user fees, that will just be passed on, will it not, to the consumer?

Dr. PECK. I would expect so, yes.

Mr. JAMES. Now we've had transgressions both in our church system, our navy—the Walkers, I believe. We still, of course, kept our navy. The S&L industry, problems there; defense subcontractors. It wasn't too many months ago that was in the headlines of all of the papers.

The FDA is aware of this. So you would expect that wherever there's money and the possibility of people making money from changing results—or bank tellers; you have to audit their procedures. Why did not the FDA have procedures in effect prior to that? You certainly couldn't be naive enough not to recognize that as a probability, that it would occur? Did you have a system in place at that time?

Dr. PECK. Well, we have always had an inspectional system. It probably has not, until this moment, been as utterly suspicious and untrusting as it is momentarily is.

Dan, would you like to expand on the tradition?

Mr. MICHELS. Yes, sir, you are correct from the standpoint that there are elements in the drug development review process that were not customarily examined and inspected as part of the routine of our oversight in bringing a product to market.

The most extreme example was the two instances of testing the innovator's brand against the innovator instead of a proper bioequivalent study.

We, frankly, had not anticipated that, and we are at fault for that. To the extent to which there are other elements of the honor system to which I alluded, we are making every effort to build that into our new program.

I must add, in going back to your original question with respect to the budget issues, this is not a free lunch. This is going to cost the agency more. These are more intensive, in-depth inspections. If additional resources are not forthcoming, they will have to be re-

programmed out of other activities. We just have a fixed pool of investigators upon which—

Mr. JAMES. Do you have adequate funds proposed by the President in his budget for his needs?

Mr. MICHELS. We have been working closely with our folks to make the estimates of what we think it is that we'll be needing for these additional safeguards.

Mr. JAMES. Thank you very much.

Back to the attorney. I didn't catch your name.

Mr. ADAMS. David Adams.

Mr. JAMES. Mr. Adams, could you tell us precisely what happened in each of those cases, if you have that information?

Mr. ADAMS. Well, to date, three individuals who were officials in drug companies have been convicted and sentenced. One individual—

Mr. JAMES. How many?

Mr. ADAMS. Three.

Mr. JAMES. Three individuals?

Mr. ADAMS. Yes, three individuals from drug companies.

Mr. JAMES. What were their levels and what companies?

Mr. ADAMS. In one company, PBI, the individual was a vice president, former vice president. He was charged with one count of providing a—

Mr. JAMES. Excuse me a minute. "Former" because of this episode or former at the time he was prosecuted?

Mr. ADAMS. I don't know what his status was at the time he was prosecuted.

Mr. JAMES. Did the culpability go beyond that? Was there implicit knowledge by the president or any other of the officers? Any evidence of that?

Mr. ADAMS. I'm not prepared to comment on that at this time.

Mr. JAMES. In other words, was there a plea bargain made to let five off the hook for the sake of one, one of those scenarios? I'm just curious.

Mr. ADAMS. I'm not aware of that.

Mr. JAMES. Okay. I didn't say that happened. I'm just using that as an example. Occasionally I understand those types of things do occur.

Did he pay a fine?

Mr. ADAMS. Yes, it was suspended jail time, a \$2,000 fine, 3 years' probation, as well as 500 hours community service.

Mr. JAMES. Two thousand for a fine was all? Is that the total amount paid in that case?

Mr. ADAMS. That was the fine for that individual.

Mr. JAMES. What did the company pay in the way of a fine?

Mr. ADAMS. There's no conviction and sentencing for the company.

Mr. JAMES. There's no what?

Mr. ADAMS. The company has not been convicted or sentenced.

Mr. JAMES. Has there a charge been made against the company at all?

Mr. ADAMS. I can't discuss that at this time.

Mr. JAMES. Well, it hasn't been made yet, and it's been how long? How many months has it been?

Mr. ADAMS. I'm not certain of when the particular conduct occurred.

Mr. JAMES. It seems to me like it would have been filed if it was going to be filed. If you went after the individual, what would take so long about going after the company?

Mr. ADAMS. I think it's been about 9 or 10 months. It would not be unusual for the Government to bring charges years after a violation occurred.

Mr. JAMES. Shall we hold our breath waiting? Do you really expect it to happen?

Mr. ADAMS. I'm afraid I can't comment on that at this time.

Mr. JAMES. That episode was what? Give us the factual scenario involved in that one PBI, in that episode? Was it faking results? Is that what it was, just a simple—

Mr. ADAMS. If you could excuse me for just a minute?

Mr. JAMES. Yes.

Mr. ADAMS. I would just like to state for the record that the investigation in this matter was carried out by the Inspector General and the Department of Justice. We did not have a direct role in the investigation and bringing the charges against these individuals.

Mr. JAMES. Thank you very much.

Let's get to the Inspector General. The Inspector General of the Department of Health and Human Services has promised a year ago to make recommendations on how regulatory mechanisms can be tightened. Have any of those recommendations been forthcoming as far as the recommendation of statutes or anything from the administration?

Mr. ADAMS. The administration is discussing internally potential legislative proposals.

Mr. JAMES. I believe that information was made available to us on November 17, 1989 in Dr. Young's testimony when he testified before Congress. It was my understanding that the Inspector General was going to make a recommendation, and I don't know of any that's been forthcoming, either legislatively or regulation-wise. Now I hear your testimony about the \$2,000 fine and no prosecution of the company.

Let's go to the other two situations. What happened in those other two scenarios?

Mr. ADAMS. In the second, there was a former president of a drug company convicted, one count of offering a gratuity.

Mr. JAMES. Like a bribery, is what you're—"offering a gratuity" is sort of like synonymous to bribery?

Mr. ADAMS. It's not necessarily the same, as I understand it. Generally—

Mr. JAMES. I'm talking generically, not legal terminology.

Mr. ADAMS. I don't know that I—

Mr. JAMES. Not brand-name—generic.

Mr. ADAMS. I don't know that I could agree with the Congressman that a gratuity is the same thing as a—

Mr. JAMES. Offering of a gratuity for an illegal act is what it was.

Mr. ADAMS. I don't believe that there was an allegation that the gratuity was offered for a specific illegal act.

Mr. JAMES. Then why was it a crime to offer the gratuity? The act itself was illegal, but what he was paying for wasn't? It must have been. It had to be.

Mr. ADAMS. I don't believe there was, as I recall, a charge as to what the quid pro quo may have been for the gratuity. Obviously, there's a concern. Gratuities are illegal. The concern is that they will influence the FDA official. I just don't recall that there was a specific allegation as to what the quid pro quo was for the money.

Mr. JAMES. What was the act for which the gratuity was given? Substitution of test materials or what? Do you know? The Inspector General, again, would be able to tell me?

Mr. ADAMS. They may. I have not been aware that any specific statement has been made as to what the act—or whether there was any act on the part of the FDA official.

Mr. JAMES. All right, thank you. Maybe we can find out some of the source question. How much was the fine and how much was the imprisonment, if any, and what was his level?

Mr. ADAMS. The fine was \$250,000. He was sentenced to 18 months in jail, all but 2 months suspended; 60 days in a work program.

Mr. JAMES. He went 2 months in jail? The balance was suspended; right? Who paid the \$250,000, the company or the individual?

Mr. ADAMS. I'm not aware of it.

Mr. JAMES. Was the company charged?

Mr. ADAMS. There are no charges—at this time the company has not been convicted.

Mr. JAMES. Did the individual pay the \$250,000?

Mr. ADAMS. I'm not aware of the source of the money.

Mr. JAMES. And what was his level with the company?

Mr. ADAMS. Formerly president.

Mr. JAMES. Formerly president? There, again, you don't know whether it was because of the charge he was former president or—

Mr. ADAMS. No.

Mr. JAMES. Okay, the third scenario—I'm running out of time. I'm talking faster than perhaps I would like to, but the reason is the time allocation.

Mr. ADAMS. We have a vice president, Par Pharmaceuticals, charged with offering an illegal gratuity to a Government employee, sentenced to 1-year suspended, \$150,000 fine, 18 months' probation, 12 months' community service.

Mr. JAMES. Twelve months' community service? Fine. What was the specific act we're talking about, the offering of an illegal gratuity? The same type of scenario that we discussed earlier probably?

Mr. ADAMS. Yes, I believe it was cash.

Mr. JAMES. Cash. I assumed it was cash and not check. At least that would be my advice if I were having to suggest the commission of an act of that nature, I would think.

Mr. ADAMS. It could be a material gift.

Mr. JAMES. My question is: what did the man do for this bundle of cash?

Mr. MICHELS. Mr. James, if I might interject here—

Mr. JAMES. Surely.

Mr. MICHELS. I think you're directly on point in terms of the concern of what was the effect of these illegal gratuities.

Mr. JAMES. No, my point is this: I want to know what kind of legislation—to me, this is inexcusable, that we don't have laws that deal more severely and sternly with this type of operation in this scenario.

I'm sorry that we had to learn by this type of mistake, and we weren't like the IRS; they audit their agents. Banks audit their tellers. Tellers, if they steal a few hundred dollars, they get a lot more of a punishment than this. In fact, I've seen people, young people, shoplifting that got worse than two of these guys in my day.

I am concerned that we don't have—and it's not your fault; I'm not blaming the administration. Maybe Congress should look at the criminal sanctions, as we did with the S&Ls. You now try to fool a bank, that goes bankrupt, and you're in trouble. I mean, you're in bad trouble. The statute of limitations has been extended. Maybe we'd best address that issue more carefully.

I don't mean to come on as a critic. It's not the administration's fault. Maybe it's something we need to look into, to be very careful.

So, I would rather get off that line of testimony—I think I've spent enough of your time on that—and go back to something that is of most concern to me. It's my opinion this can happen with brand-names as well as generics. I don't see the distinction in the market as to the possibility of this type of activity occurring. I don't see any great sanctification of a brand-name as opposed to a generic. I'm concerned about both.

A brand-name is simply, in many cases, more expensive because of the research and development that went into the product and because of the patents involved and because of the advertisement of that name—is why it demands, and must receive, a larger cost at first, until some of that research and development has been recouped. We all know that's the reason.

But, Dr. Peck had suggested earlier—and this is one other thing I want to ask before I terminate my questioning. You said, discuss with your physician whether to use a generic or a brand-name. It's my understanding that if the generic is a true generic, there should be no necessity for that discussion.

I believe Mr. Haddad was trying to suggest that. In fact, based on the training that Mr. Haddad—and I hope I'm pronouncing that correctly—suggested, he said there was an economic motivation sometimes between the information a physician receives. I assume what he's talking about is the pharmaceutical salesman for many PPs is the primary source of information, his PDR, physician's desk dictionary.

If that be the case with these two courses in medical school and the 5 years as a pharmacist, then, Dr. Peck, would you not agree that perhaps that isn't the person to discuss it with as far as whether to use a generic or a brand-name? I don't understand that comment or advice if those facts are true. Would you care to comment on that?

Dr. PECK. Certainly. First of all, let me say that the agency does not take a position on the practice of medicine. We feel that our purview is to ensure that drugs that are marketed are safe and effective, and that the labeling is consistent with their expected actions.

It is a long-held tradition in this country that the final contract between the health care system and the patient is consummated by the physician and the patient. After all, it's the physician who takes the medical-legal responsibility for the outcome of therapy and stands to be sued if it fails because of his failure.

So, I—

Mr. JAMES. Maybe that's an unfair responsibility to put on them. Also the drug manufacturer, the generic, can be sued, too. The manufacturer, if there is a deviation—we're talking about only the narrow scope of whether you recommend a generic or a brand-name. It would seem to me that the physician could not be held liable if the FDA did its job, and it worked perfectly; the system worked perfectly, because there shouldn't be a generic on the market that isn't the same quality, meets the same governmental standards as the brand-name.

That's the point I'm making. In other words, aren't we putting a burden on the doctor to pretend that the doctor should know? How would he know? He's not a laboratory. He can't test them and do an objective test as to whether or not this generic is equal to—he could have all the theories in the world, but unless he has a \$10 million laboratory, the millions of dollars it takes for a laboratory, he cannot come to an informed conclusion as to a specific drug, nor would I assume that he has the statistical basis from seeing his patients to make a competent, informed decision as to the different metabolic influences on the different patients. In order to come to that conclusion, you have to have total control of the intake of those patients, their food intake, et cetera.

I don't see how a physician could be expected to make that evaluation, is my point, regardless of tradition. I just don't see how he could—I don't care what a genius he may be, I just don't know how we could expect that. That's really my point, not to be critical in any way of the physicians; indeed, I am not; I have a great deal of respect for the profession—they save our lives—as I do for the pharmacist.

I'm only saying that to even assume or to allude to the suggestion that that profession can answer that question is asking too much of them in that sense. Would you disagree with that?

Dr. PECK. Well, respectfully, some I think. I have practiced medicine myself, and my colleague on my left continues to practice. He may want to have a comment here.

It's a long-held ethic that the physician and the patient have a complete, although this is not always the case, have a complete open line of communication between them. The physician should know what the patient is taking. The physician could possibly know about a product defect that even the agency had not discovered yet.

Mr. JAMES. I see what you're saying. In other words—I understand—because the FDA, that's one other area I did not have time to cover. I see what you're saying. If they heard about a potential problem, subject to that qualification—

Dr. PECK. Yes.

Mr. JAMES.[continuing] if they have knowledge by hearsay, or whatever, from some other source, I would expect the doctor to intervene, what I mean as far as otherwise forming an opinion.

Okay, I understand. Thank you. I would agree with you certainly on that.

The next, my last question—and I said my other one was my last, but the last question is: what are we doing about disseminating—and anyone can answer this—are we disseminating information to all the doctors that are practicing as soon as we know it, or suspicious circumstances, or what is the level of communication we have to the individual doctors to make sure we're not depending on their organizations to do it, but it's the Government telling them to avoid the scenario of 160,000 prescriptions—and to the pharmacists, for that matter—160,000 prescriptions of a defective drug. How are we answering that problem? Does anyone want to answer that?

And that's my last question. Thank you all so much for your enlightening testimony. Thank you.

Mr. BURLINGTON. The agency uses a number of tools to disseminate information to the health professionals. One is through the organizations of health professionals. We update them on an online basis the day that a story breaks in one of these generic drugs. Because of speed of communication, we also use the popular press, in addition to which we have the FDA drug bulletin which goes to virtually every physician and most pharmacists in the country. It has carried, and will continue to carry, periodic stories. Also, as was previously mentioned, we have a monthly column in the Journal of the American Medical Association that Dr. Stewart Nightingale disseminates information to physicians.

We think these tools do get the story out to the prescribing physicians and the dispensing pharmacists.

Mr. JAMES. But you're depending on unofficial organizations rather than communicating with them directly?

Mr. BURLINGTON. Well, at least one of those tools, the drug bulletin, the FDA sends that directly to the physicians and pharmacists.

Mr. JAMES. You do that in those cases?

Mr. BURLINGTON. Yes.

Mr. HADDAD. They have a very effective recall system where, if you have a real tragedy, they can trace the—because of the numbers in the labeling—right back to where all the pills are. They can pull them right off the market.

Mr. JAMES. Were you here and heard the testimony of—I don't know whether it's true or not

Mr. HADDAD. Yes, the chlorothenical situation.

Mr. JAMES. Was there any truth to that?

Mr. HADDAD. There's a lot of truth in chlorothenical.

Mr. JAMES. Then that didn't work, then?

Mr. HADDAD. No, but that was many years ago. What happens now is, if there is a recall, you have an immediate pulling-off right down to the pharmacist's shelf. It doesn't get every prescription in the household, Mr. Michels has a pretty rapid system.

Mr. JAMES. That makes me feel much better, if and when I take the next prescription. I do appreciate that. That would scare a lot of people, if they thought that was possible now. We don't want people to be fearful unreasonably, but be concerned about the problems we do have.

Thank you so much.

Ms. LLOYD. Thank you very much, Mr. James, for your excellent questions and fine thoughts.

I want to get back to one point maybe I missed out on. We were talking about illegal gratuities. Are there legal gratuities? I want to set the record straight on that.

Mr. ADAMS. I'm not aware of anything that I could characterize as a legal gratuity. "Gratuity" is a legal term.

Ms. LLOYD. I have a great deal of admiration for the Food and Drug Administration. I brought that out in my opening testimony; that I realize that you have worked under very severe circumstances. You've had a lot to do with less employees than you need. You're a very dedicated organization.

But, at the same time, I'm going to say to you that I think it is the responsibility of the Food and Drug Administration to set up the penalties, to make sure they are in force. I don't think this is a role that Congress—if we have to, we will, but I certainly hope that we do not have to take on this responsibility for you.

We certainly will be following this up in later hearings later on in the year.

The one question that I had left of you, Dr. Peck: I'm concerned about the independent laboratories that test the bioequivalency of generic drugs. This is a great concern. Are you sure that the labs who are being paid directly by the drug firms for the testing—do you feel that they have been inappropriately influenced by the drug companies?

Dr. PECK. Well, at the instant I have no knowledge if they have been inappropriately influenced. However, we have some concerns that we are investigating. We have a concern about the prospect that an independent laboratory could be paid in any other way than a fee for service; for example, could hold some form of equity in the product that they're testing. We're looking into that matter.

Ms. LLOYD. I think the message should go out that this greed will not be tolerated. Do you feel that you need more authority to address this situation?

Dr. PECK. I think until we have investigated the matter thoroughly and know what the possible universe of inappropriate or illegal actions there, I would want to withhold a recommendation.

Ms. LLOYD. Well, I will respect that.

Dr. PECK. I think that Mr. Michels may have a little addition to this answer.

Ms. LLOYD. Mr. Michels?

Mr. MICHELS. Frankly, at this time our first concern has not been focused on independent laboratories, but on the sponsors of the applications themselves, because that's where we've detected the fraud. In other words, the wrong sample was shipped to the laboratory. They were completely unaware of what it was that they were testing, that it was, in fact, the wrong material or that information would be misconstrued.

We are carefully looking at the matter of financial remuneration for these kinds of things. I must point out that it's, at least under the present circumstance, quite permissible for a firm to do its own in-house bioequivalence testing, such that the whole task would be undertaken within the corporate umbrella and not be done by an independent laboratory. Just addressing issues of concern about an

independent laboratory would not necessarily close all of the potential gaps that might exist there.

The issue is, frankly, a complex one. There are issues of economics and business relationships that we need to research and really begin to understand.

Ms. LLOYD. What is your recommendation on how to deal with this, the in-house testing on bioequivalency or by an independent lab?

Mr. MICHELS. Well—

Ms. LLOYD. What should we do with this?

Mr. MICHELS. Well, I think we are doing the first and most important thing, and that is we have in process the regulation to require the retention of bioequivalent samples no matter who does them, such that we can lay hands on them, backtrack, and determine whether, in fact, this was the authentic material or whether a fraud was perpetrated.

That's irrespective of whether the study was done in-house or by an independent group.

I, like Dr. Peck, however, with respect to the nuances of financial relationships—please forgive us, at least me. My focus has been longstanding within the agency as a compliance officer and ex-investigator, looking at the technology and, for example, assuring that good manufacturing practices are being complied with.

We've got a very steep learning curve here in some of the elements that we need to look at. I assure you that if we believe that we do not have the authorities to close an apparent loophole in the honor system, we'll be back.

Ms. LLOYD. Well, this is an ongoing concern of this committee. We look forward to being back with you before the end of this year to review this situation. I thank you for that.

One final question for you, Mr. Haddad. You stated the guilty pharmaceutical employees, the guilty ones had paid light fines.

Mr. HADDAD. Yes.

Ms. LLOYD. Who were you referring to? Do you think they should be given stiffer fines?

Mr. HADDAD. I'm a hawk on this. I'm a liberal on my politics and a hawk on this thing. I just felt that the thing that the Congressman was addressing—I thought the fines were light, and I thought the penalties—the penalties of law are very stiff. There's something called a Parke decision. If anybody in your firm messes, the guy signs a piece of paper, at the top, the president, the CEO is liable. There are very stiff penalties.

But the court enforced these penalties in the beginning in a very, what I felt was, a light way. However, the information I do not have is the question that you are alluding to, whether or not there was a chain of command; whether they wanted to work something out. Maybe the plea bargaining was to build a foundation for something else. I'm not aware of any of those things, but I feel like some of the fines were in the early days quite light.

Mr. JAMES. Maybe the fine were stiff in regard to the individual that was actually fined; I don't know. What I'm saying is, from the nature of the culpability of the acts described to me by the news media, et cetera, a total composite of the fines and sentencing that I've heard, regardless of numbers or innocents or guilty—there was

at least one guilty man in the group; we know that—guilty of taking the risk of thousands, if not millions, of people's lives.

Mr. HADDAD. Well, the judge in sentencing—I read his sentencing report last night, and he said, in sentencing, he took in the fact that safety and health have not been injured, but I still hold to my position that I feel that penalties that were handed down were not tough enough.

Mr. JAMES. Well, there's little or no way I would assume that he—maybe because it was a new drug and it hadn't been dispensed yet?

Mr. HADDAD. Now he is sitting on the grand jury, too, I think. He said that there are a lot of brand companies and generic companies that are going to be coming down the line with further indictments and things, or he hinted at it, but he said the penalties that the had imposed were—he didn't use the word "light," but he said they were appropriate and—

Mr. JAMES. What's the maximum sentence they could have received for one act—

Mr. HADDAD. They vary. I don't know all the statutes, but some of the statutes are very tough.

Mr. JAMES. Five years?

Mr. HADDAD. You can go 15, 20 years.

Mr. JAMES. That's what I wanted to address. Do you think the need to have new laws or tougher laws—or was that a matter of one individual judge's light sentencing, or not light, possibly light.

Mr. HADDAD. He may be doing something else that we don't know anything about. The U.S. Attorney may be building a case. You don't know those circumstances. I think they are very tough laws. I happen to be a hawk and favor tougher than what they are and more penalties for the FDA to use internally, but I'm not ready to address the statutes. I think the Dingell committee is looking at that right now.

Mr. JAMES. So, perhaps the FDA can make recommendations as to increased severity, if that be the case, to the appropriate committee? I would assume that you would do that, to make it very difficult to commit that kind of heinous act.

Thank you very much.

Ms. LLOYD. I've just been told we're supposed to clear out of this room a little bit after 12. I do thank you gentlemen for very valuable testimony.

The last panel includes Dr. David Cobb of Lexington, Kentucky, president of the American Pharmaceutical Association, and Dr. Charles White of Lexington, Tennessee, who's a family practice physician and a member of the Tennessee Medicaid Formulary Advisory Board.

Gentlemen, we thank you for being here. Dr. Cobb, if you will summarize, we would appreciate it. We do have your complete testimony for the record.

STATEMENT OF R. DAVID COBB, PHARM.D., PRESIDENT,
AMERICAN PHARMACEUTICAL ASSOCIATION

Dr. COBB. In the interest of time, you have my complete testimony. I will make it very, very brief. I think that's what you're saying to me, is we have no time. It's all in front of you.

I think I would just call your attention to page 5 and 6 of my testimony, and very quickly tell you that we believe the generic drug industry has had some problems. They have been solved. We're still working on it, as you've heard previous testimony.

We think, however, there are some things that need to be done, and those particular things are summarized on 5, particularly on page 6. Specifically, we believe that the pharmacists can better serve the public if the following additional information were required on the label of all multi-source drug products, including the FDA Orange Book rating; the name of the manufacturer, as well as that of the distributor; a list of all ingredients, not just active ingredients.

I think on page 7, the conclusion summarizes the American Pharmaceutical Association's position on generic drugs. We believe the American public should not let recent investigations undermine the legitimacy of the use of generic drug products. Patients who take generic products should not stop using them. Patients who are not prescribed brand-name products should not insist on them, but rather consult with your physician or pharmacist to assure themselves that they're receiving the most cost-effective drug product for the condition.

We still have confidence, as the pharmacists of this Nation, in the generic drug industry. We have a saying in Kentucky, which most people have, about bad apples in a barrel. I don't believe the couple of bad apples in this barrel have spoiled the whole industry. We still have confidence in them.

It is obvious to me in some of the testimony given here today that the Chair would benefit greatly from an understanding of some of the substitution laws that are in place in this country. I would like to volunteer our association to help acquaint you with those. Some of the last discussion about physicians, patients discussing their drug therapy with their physicians and their pharmacists—in many cases—

Ms. LLOYD. I really want you to elaborate on that; okay? About discussing this with pharmacists.

Dr. COBB. All right. In, I believe, approximately—don't hold me to these numbers; my staff will prepare the numbers and give you some direct information—but I believe in about 28 States the substitution of a generic drug is mandatory, the least expensive drug. In most States generic substitution—I believe now in all 50 States there are generic substitution laws that mandate some form of substitution; if not mandated, suggested highly.

Many times there is no choice. The law requires in the State of Kentucky for me to dispense the least expensive product I have in stock if the drug is not in the negative formulator—it has an A rating—we must substitute. We have no choice.

The physician can still discuss with the patient the right to not dispense the generic, but the default value is the generic drug, not

the brand-name, to begin with. If the physician just writes the brand-name drug, they will get the least expensive drug in stock that I have. That is the case in many States.

I don't believe Mr. James understood that well, and I think it would be helpful if he did that before he looked at this.

I think it's important to note that I was just handed, while I was sitting here, released February the 28th—the latest Gallup Poll says that, "Pharmacists remain the highest rated profession in America in terms of honesty."

Ms. LLOYD. You did a lot better than Members of Congress.

Dr. COBB. I will not comment on that.

Ms. LLOYD. I didn't expect you to.

Dr. COBB. They rate pretty high, too, in my mind.

We do have a high ethical standards. Honestly, I believe that many patients can benefit greatly in their generic drug therapy if they will talk to their pharmacist.

We, like anybody else, have people who don't do what they're supposed to do. I would like to remind this group, particularly from the early testimony of the consumers, that when I graduated from pharmacy school, which seems ancient now, and it has been 20 years ago, but 20 years ago I was taught to say to a patient who asked me anything about a drug, I was to say nothing. My ethical standards required that I did not divulge the name, what it was used for, or anything of that nature.

It has only been in the last 15 years that we even teach our graduates to talk about these things. This is something new. I think sometimes that gets lost in the shuffle.

We're still learning. Unfortunately, we have practitioners who graduated more than 20 years ago, or more than 15 years ago, who still need to do that better, but we're getting there. We're working at it, and hopefully we'll someday become perfect; I rather doubt it.

Ms. LLOYD. Thank you. I appreciate that.

[The prepared statement of Dr. Cobb follows:]

**Statement
of the
American
Pharmaceutical
Association**

The National Professional Society of Pharmacists

ON
"QUALITY OF THE GENERIC
DRUG SUPPLY IN THE UNITED STATES"

PRESENTED IN CONJUNCTION
WITH THE
HEARING HELD BY THE
SUBCOMMITTEE ON HOUSING AND
CONSUMER INTERESTS
OF THE SELECT COMMITTEE ON AGING

ON
MARCH 1, 1990

SUBMITTED BY
R. DAVID COBB, PHARM.D.



American Pharmaceutical Association
2215 Constitution Avenue, N.W.
Washington, D.C. 20037

APhA

(202) 628-4410

AS THE PRESIDENT OF THE AMERICAN PHARMACEUTICAL ASSOCIATION (APHA), THE NATIONAL PROFESSIONAL SOCIETY OF PHARMACISTS, I AM PLEASED TO HAVE THIS OPPORTUNITY TO TESTIFY ON THE QUALITY OF THE GENERIC DRUG SUPPLY IN THE UNITED STATES. I AM JOINED BY DR. ARTHUR H. KIBBE, APHA'S DIRECTOR OF SCIENTIFIC AFFAIRS.

SKYROCKETING HEALTH CARE COSTS HAVE PUT A TREMENDOUS BURDEN ON INDIVIDUAL AMERICANS, AS WELL AS THE FEDERAL GOVERNMENT, AND TAKE AN EVER INCREASING PORTION OF THE GROSS NATIONAL PRODUCT. THIS BURDEN HAS BEEN FELT MOST BY THOSE SUCH AS THE ELDERLY WHO ARE ON FIXED INCOMES. BECAUSE MOST MAJOR MEDICAL EXPENSES ARE COVERED BY PRIVATE INSURANCE OR GOVERNMENT PROGRAMS THE LARGEST OUT-OF-POCKET EXPENSE IS OFTEN THE COST OF MEDICINES. BUT IN MOST CASES, THE NEWER, MORE EXPENSIVE DRUGS REPLACE EVEN MORE COSTLY METHODS OF TREATMENT SUCH AS SURGERY. SO, IT IS IMPORTANT TO BALANCE THE COST OF PHARMACEUTICALS AND PHARMACY SERVICES WITH THE BENEFIT THEY PRODUCE. HOWEVER, LET ME ASSURE THIS CONGRESSIONAL COMMITTEE THAT PHARMACISTS ARE KEENLY AWARE OF THE PART DRUG PRODUCT COSTS HAVE PLAYED IN CONTRIBUTING TO THE OVERALL INCREASES IN HEALTH CARE COSTS.

PHARMACISTS CAN PLAY AN IMPORTANT ROLE IN CONTROLLING DRUG PRODUCT COSTS WHEN THEY ARE GIVEN TOOLS LIKE THE ABILITY TO USE FORMULARIES AND THE FREEDOM TO SELECT THE MOST COST EFFECTIVE MEDICATION FROM AMONG THOSE AVAILABLE FROM MULTIPLE SOURCES. (SEE ATTACHED "REPORT OF THE TASK FORCE ON THE COST EFFECTIVENESS OF PHARMACEUTICALS AND PHARMACY SERVICES.")

AN IMPORTANT METHOD PHARMACISTS USE TO HELP REDUCE THE COST OF NECESSARY DRUG TREATMENT, ESPECIALLY THOSE DRUG PRODUCTS USED FOR THE TREATMENT OF CHRONIC CONDITIONS, IS TO SELECT A QUALITY GENERIC DRUG PRODUCT.

APHA HAS BEEN INVOLVED WITH DEVELOPING INFORMATION FOR PHARMACISTS REGARDING THE RELATIVE QUALITY OF GENERIC DRUG PRODUCTS SINCE 1971. IT IS NOW POSSIBLE TO ACCURATELY MEASURE HOW MUCH ACTIVE INGREDIENT IS ABSORBED INTO THE BODY FROM A DOSAGE FORM AND THE SPEED WITH WHICH THAT ABSORPTION OCCURS. WHEN TWO PRODUCTS SHOW THE SAME PATTERN OF

ABSORPTION, THEY ARE CONSIDERED BIOEQUIVALENT. PRODUCTS THAT HAVE BEEN PROVEN TO BE BIOEQUIVALENT ARE CONSIDERED TO HAVE THE SAME POTENTIAL FOR THERAPEUTIC BENEFITS AND CAN BE USED INTERCHANGEABLY.

I CANNOT TAKE TIME NOW TO DESCRIBE IN DETAIL THE PROCESS OF BIOEQUIVALENCY TESTING. HOWEVER, THE SCIENTIFIC BASIS OF BIOEQUIVALENCY TESTING HAS BEEN WELL ESTABLISHED AND IS UNIVERSALLY SUPPORTED THROUGHOUT THE SCIENTIFIC COMMUNITY.

APHA COMMENDS CONGRESSMAN DINGELL AND THE HOUSE SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATION FOR THEIR EFFORTS TO EXPOSE SPECIFIC INSTANCES OF ILLEGAL AND IMPROPER ACTIVITIES. NOTWITHSTANDING THESE FINDINGS, THE PHARMACISTS OF THE NATION STILL HAVE A GREAT DEAL OF CONFIDENCE IN THE QUALITY OF THE MAJORITY OF GENERIC DRUG PRODUCTS ON THE MARKET TODAY. APHA RECOGNIZES THAT ONE SHORT TERM EFFECT IS THE PUBLIC'S CONFIDENCE IN THE GENERIC DRUG INDUSTRY AND GENERIC DRUG PRODUCTS HAS BEEN REDUCED AS DEMONSTRATED BY THE RESULTS OF A RECENTLY COMPLETED PUBLIC OPINION POLE. (GENERIC DRUG USERS PERCEPTION OF THE INDUSTRY, THE

GALLUP ORGANIZATION, INC., MARKETING AND ATTITUDE RESEARCH, PRINCETON, NJ, PREPARED FOR LEDERLE LABORATORIES, DEC., 1989.) HOWEVER, APHA BELIEVES THAT THE SUBCOMMITTEE'S EXPOSURE WILL EVENTUALLY LEAD TO A STRONGER AND MORE RESPONSIVE GENERIC DRUG INDUSTRY AND REASSURE THE AMERICAN PUBLIC OF THE QUALITY OF ALL DRUG PRODUCTS IN THE FUTURE.

ONE WAY APHA RESPONDED TO THE CRISIS CONCERNING THE INTEGRITY OF THE GENERIC DRUG APPROVAL PROCESS WAS TO IMMEDIATELY FORM A "BIOEQUIVALENCY WORKING GROUP" COMPOSED OF PHARMACY PRACTITIONERS AND PHARMACEUTICAL SCIENTISTS. THE GROUP DELIBERATIONS RESULTED IN GUIDELINES FOR PHARMACISTS TO USE WHEN MAKING DRUG PRODUCT SELECTION DECISIONS. APHA ALSO PREPARED A FACT SHEET ON GENERIC DRUG PRODUCTS THAT PHARMACISTS CAN DISTRIBUTE TO THEIR PATIENTS. WE MAILED THIS FACT SHEET AND RELATED INFORMATION TO 120,000 PHARMACISTS IN THE UNITED STATES. (BOTH OF THESE DOCUMENTS ARE ALSO ATTACHED TO THIS TESTIMONY.)

APHA IS NOW IN THE PROCESS OF PREPARING A MORE COMPLETE BROCHURE REGARDING GENERIC DRUGS TO ASSIST THE NATION'S PHARMACISTS IN EXPLAINING GENERIC DRUG PRODUCTS AND THEIR APPROPRIATE USE. WE INVITE THE COMMITTEE TO JOIN US IN THIS ACTIVITY TO INSURE THAT THE INFORMATION GETS THE WIDEST POSSIBLE DISTRIBUTION TO THE GENERAL PUBLIC.

HOWEVER, APHA DOES HAVE SOME CONCERNS THAT WE HOPE THE COMMITTEE WILL HELP CONGRESS ADDRESS THROUGH LEGISLATIVE ACTION. ALTHOUGH THE VAST MAJORITY OF GENERIC DRUG PRODUCTS AVAILABLE TO THE PUBLIC ARE APPROVED BY THE FOOD AND DRUG ADMINISTRATION (FDA), THERE ARE MANY DRUGS THAT WERE MARKETED PRIOR TO 1938 WHICH DO NOT REQUIRE FDA APPROVAL PRIOR TO SALE. AS A RESULT, THERE ARE FEW TESTING REQUIREMENTS FOR THEIR GENERIC VERSIONS, MAKING IT DIFFICULT FOR A PHARMACIST TO OBTAIN RELIABLE BIOEQUIVALENCY INFORMATION ON THE GENERIC VERSION OF THESE DRUG PRODUCTS. WITHOUT SUCH INFORMATION, SELECTING QUALITY GENERIC EQUIVALENTS OF THESE PRE-1938 DRUGS IS MORE DIFFICULT THAN FOR THOSE DRUGS THAT HAVE

GAINED FDA APPROVAL AND FOR WHICH THERE IS A KNOWN BIOEQUIVALENCY RATING. IN ADDITION, PHARMACISTS LACK EASY ACCESS TO CERTAIN KEY INFORMATION THAT COULD BE PROVIDED BY THE MANUFACTURER OF THE GENERIC DRUG PRODUCTS.

PHARMACISTS COULD BETTER SERVE THE PUBLIC IF THE FOLLOWING ADDITIONAL INFORMATION WERE REQUIRED ON THE LABEL OF ALL MULTI-SOURCE DRUG PRODUCTS:

- A) THE FDA ORANGE BOOK RATING;
- B) THE NAME OF THE MANUFACTURER, AS WELL AS THAT OF THE DISTRIBUTOR;
- C) A LIST OF ALL INGREDIENTS, NOT JUST ACTIVE INGREDIENTS.

THE COMMITTEE COULD PROVIDE THE NATION'S PHARMACISTS A GREAT SERVICE IN HELPING THEM ASSURE THE PUBLIC OF ACCESS TO HIGH QUALITY COST-EFFECTIVE GENERIC DRUG PRODUCTS BY LEGISLATIVELY MANDATING THAT THIS INFORMATION BE INCLUDED IN THE OFFICAL LABELING OF ALL MULTI-SOURCE DRUG PRODUCTS.

IN CONCLUSION, APHA BELIEVES THE AMERICAN PUBLIC SHOULD NOT LET RECENT INVESTIGATIONS UNDERMINE THE LEGITIMACY OF THE USE OF GENERIC DRUG PRODUCTS. PATIENTS WHO TAKE GENERIC PRODUCTS SHOULD NOT STOP USING THEM. PATIENTS WHO ARE NOT PRESCRIBED BRAND NAME PRODUCTS SHOULD NOT INSIST ON THEM BUT RATHER CONSULT WITH THEIR PHYSICIAN AND PHARMACIST TO ASSURE THEMSELVES THAT THEY ARE RECEIVING THE MOST COST EFFECTIVE DRUG PRODUCT FOR THEIR CONDITION.

THANK YOU FOR THE OPPORTUNITY TO BE HERE. I WILL BE HAPPY TO ANSWER ANY QUESTIONS YOU MIGHT HAVE.

"THE PRECEDING IS THE BASIS FOR DR. COBB'S REMARKS. HE MAY DEPART FROM THIS PREPARED TEXT. THE ACTUAL TEXT OF THE ADDRESS AS DELIVERED WILL BE AVAILABLE FROM APHA."

THE TASK FORCE ON THE COST-EFFECTIVENESS OF
PHARMACEUTICAL PRODUCTS AND PHARMACY SERVICES

Final Report

October, 1989

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EXECUTIVE SUMMARY

The Task Force on the Cost-Effectiveness of Pharmaceutical Products and Pharmacy Services was formed by the American Association of Colleges of Pharmacy (AACP), the American Pharmaceutical Association (APhA), and the Pharmaceutical Manufacturers Association (PMA) in 1987.

The charge to the task force was to assemble and review existing research findings on the cost-effectiveness of pharmaceutical products and pharmacy services, summarize the key findings, and identify areas where data do not exist and further research might be conducted. The emphasis of the project was to evaluate the cost of drug therapy when medicines are prescribed, considered, dispensed and administered compared to other forms of acute or chronic treatment such as surgery, testing or institutionalization. The Task Force arrived at the following recommendations and conclusions after a review and analysis of current literature (1986-89):

Recommendations

Recommendation 1

Because of the evolving nature of economic evaluation research, policy makers must approach research findings with caution and balance the weight given to such research with value

judgments on the patient benefits of pharmaceutical products and pharmacy services.

Recommendation 2

Research focusing on the economic evaluation of pharmaceuticals should continue, with emphasis on widely used classes of drugs and those likely to be unusually costly to the health care system.

Recommendation 3

Research focusing on the economic evaluation of pharmacy services should continue, with emphasis on the contribution of pharmacy services in ambulatory care settings, and upon multisited studies designed to overcome the deficiencies on anecdotal and single-site studies.

Recommendation 4

Investigators should be encouraged to develop and carry out studies to determine the combined economic impact of pharmaceuticals and pharmacy services.

Conclusions

The Task Force finds it easy to conclude that the contributions of pharmaceuticals and pharmacy services to society far exceeds their cost. There is little doubt that society has

implicitly reached the same conclusion, given the frequency with which drugs are used in all areas of health care. Nevertheless, the widening gap between the costs of health care and the amount that society is prepared to pay, either through government or other third-party payors, has created a desire to evaluate all health care services and technologies from an economic standpoint. Pharmaceutical interventions such as vaccines, antibiotics, and H₂ antagonists frequently have a favorable economic profile, often serving to actually reduce the total costs of health care. Furthermore, this net economic benefit is sometimes so obvious (e.g. polio vaccine) that economic evaluations are unnecessary. There are two settings in which economic evaluations are particularly useful: (1) complex therapeutic or preventive dilemmas where the economic impact of alternative drug and non-drug interventions are unknown and (2) issues of identifying priority patient population subsets for receipt of high cost, highly effective drugs that nevertheless result in a net increase in total health care costs (e.g. antihypertensives, thrombolytic agents).

The war over increasing health care costs is fought on specific battle grounds such as Medicaid programs, third party drug programs, and health care institutions all over the country. The demand for data to demonstrate the economic value of particular drugs and of particular pharmacy services will continue. And there is an obligation to attempt to provide the best data possible to meet such demands.

On the other hand, the clamor for more definitive economic studies is often a way of deferring or avoiding decisions that cannot be decided on technical factors alone; value judgments are required. If a new pharmaceutical becomes available that offers a cure for a condition where none existed or if a pharmacy service can provide relief where no relief was available before, what is an acceptable price for such a product or services? The methods of economic evaluation provide necessary and powerful input to that decision, but can not provide an unequivocal answer. The integration of value judgments with the results of high-quality economic evaluations is critical to responsible patient care and public policy making. It is from this perspective that the Task Force's recommendations should be considered.

PHARMACY TODAY

Guidelines for Pharmacists Performing Product Selection

■ Dispensing Decisions

APhA's Bioequivalency Working Group recommends that pharmacists consider the following factors when selecting drug products to be dispensed to their patients. Not all of these factors will apply to each situation nor are they of equal weight. We believe if pharmacists consider these points as part of the professional judgment process when making drug product selections, it is likely that the best interests of the patients will be served. It is the responsibility of the pharmacist to use professional judgment in selecting the product.

- 1) ■ **State Rules and Regulations.** All states have legal requirements that address the issue of drug product selection. Pharmacists should be cognizant of these requirements and how they may impact their role in drug product selection. State regulations also might provide information and guidance in drug product selection through positive or negative formularies.
- 2) ■ **Bioequivalency Information/Orange Book Ratings.** Only products with proven bioequivalency should be selected to be dispensed in lieu of the innovator product. Products being dispensed in response to a prescription drug order that is written generically should be expected to produce a therapeutic benefit for the patient at a reasonable cost. Products that are listed in the FDA's *Approved Drug Products and Therapeutic Evaluation*¹ (the Orange Book) as "K" rated should be selected when such products are available. For pre-1938 drugs, the selection should be based on data obtained from the literature, because bioequivalency testing is not required by the FDA for these drug products. FDA's review of the applicant's bioequivalency study is available under Freedom of Information (FOI).²
- 3) ■ **Dosage Form.** The type of dosage form should be considered whenever one drug product is selected from among multisource drug products. This is especially true with extended or delayed release medications. The Orange Book does not rate any different dosage forms as therapeutically equivalent.

- 4) ■ **Previous Drug Use.** Two questions should be considered regarding previous drug product usage. First, is the prescribed drug a continuation of already successful therapy? If it is, only a bioequivalent product should be selected, and the impact of any change in source of the medication should be considered. The pharmacist should also know which product the patient was using previously, including any medications in the hospital if the patient was recently discharged. Second, was the original product dispensed a generic product? If so, preference should be given to continuing to dispense the same generic product from the same source.
- 5) ■ **Patient Status.** The pharmacist should consider how well controlled the patient is and how susceptible that patient might be to small changes in drug absorption. If a patient has labile control or has experienced great difficulty in achieving control, the pharmacist should continue therapy with a product from a single source throughout therapy.
- 6) ■ **Diseases.** The seriousness of the disease and its potential impact on the patient may influence the pharmacist's willingness to change products.
- 7) ■ **Drug Class or Category.** Drugs with narrow therapeutic ranges and with known clinically significant bioavailability problems should be substituted with care and/or after discussion with the prescriber.
- 8) ■ **Cost.** The cost of the product, while an important consideration, should be a secondary consideration in selecting among products judged by the pharmacist to be bioequivalent.
- 9) ■ **Patient Opinion.** An informed patient, cooperating with a physician and pharmacist in his or her drug therapy, is an important element in ensuring the best possible therapeutic outcomes. The pharmacist should take into account the patient's needs when selecting from multisource drug products and inform the patient of any potential consequences associated with alternate product selections.

■ Purchase Decisions

APhA's Bioequivalency Working Group recommends that pharmacists consider the following factors when purchasing products from multisource vendors. Not all of these factors are of equal importance in each purchasing decision, but all are worthy of consideration.

- 1) ■ **Current State Laws and Regulations.** States have legal requirements that address the issue of drug product selection. Some states have positive or negative formulary systems that place regulatory restrictions on the products considered therapeutically equivalent. The state formulary may not always be in agreement with classifications listed in the FDA's Orange Book. Therefore, pharmacists should be familiar with both. Some states also have regulations which define the role of the pharmacist, physician, and patient in the drug product selection process.
- 2) ■ **Bioequivalency Information/Orange Book.** Products shown to be bioequivalent through reference to the Orange Book or other reliable source of bioequivalency information are preferred. Purchase decisions for drugs marketed prior to 1938 should be based on data obtained from the literature or the manufacturer, because bioequivalency testing may not be required by the FDA for these drug products.
- 3) ■ **Drug Category.** Greater attention should be given to purchasing strategies for drug products used for serious or life-threatening diseases and in situations where therapeutic activity of the product is confined to a narrow range of biologic fluid concentration.
- 4) ■ **Availability.** A continuous supply from the same manufacturer is essential even in the event that the distributor has changed to ensure that refills of prescriptions will contain the same product as originally dispensed. However, in those instances when the

manufacturer of a generic drug product has to be changed, care should be exercised to ensure that the new drug product is equivalent to the formerly stocked drug product.

- 5) ■ **Supplier's Reputation.** The reputation of the manufacturer in terms of its ability to adhere to good manufacturing practices (GMP) that ensure that each dosage form is manufactured correctly and in a consistent manner is an important consideration. When purchasing a product from a distributor rather than directly from the manufacturer, the procedure used by that supplier in selecting manufacturers for multi-source products is also an important consideration. Establishment Inspection Reports and recall reports³ are available from FDA through a Freedom of Information (FOI) request. These are valuable tools in this decision.
- 6) ■ **Cost.** Cost of the product is an important consideration for both the patient and the pharmacy.

References

1. A subscription to the "Orange Book," which includes the 1990 *Basic Manual* and monthly supplements, is available for \$91 from the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402-9372. A subscription to the *USP-DI, Approved Drug Products and Legal Requirements*, Volume III, includes one book and monthly updates. It is available for \$59 from the U.S. Pharmacopeial Convention, Inc., Order Processing Department, 12601 Twinbrook Parkway, Rockville, MD 20852.
2. Freedom of Information Staff, HFW-35, Food and Drug Administration; 5600 Fishers Lane, Rockville, MD 20857; (301) 433-6310.
3. Recall/Regulatory Analysis, P.O. Box 6353, Silver Spring, MD 20906; (301) 460-8821. ☐



**American
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*The National Professional
Society of Pharmacists*

APhA

John A. Gans, PharmD
Executive Vice-President

R. David Cobb, PharmD
Chairman of the Board

Dear Colleague:

Are your patients concerned about the quality and effectiveness of generic drugs?

Does the public understand the health care benefits provided by pharmacists?

Today's headlines call into question the safety and effectiveness of generic drugs and the Food and Drug Administration (FDA) process that approves them for distribution. Are you prepared to respond to your patient's questions?

The enclosed fact sheets on generic drugs have been prepared for you as a service of the American Pharmaceutical Association (APhA). One offers a summary of current activity and background information. The other can be copied and used as a generic drug information flyer for your patients — a way for you to help them make sense out of what they are hearing and reading.

For further help in sorting out the issues, I encourage you to read regularly *Pharmacy Today*. The enclosed sample covers the generic drug crisis, as well as the latest on APhA's efforts to resolve discriminatory pricing and the proposed restricted distribution of Sandoz's new drug Clozaril which would exclude most pharmacists. And don't miss the list of drug and medical equipment recalls on the back page — a regular feature of *Pharmacy Today*.

We at APhA have committed to a massive new APhA consumer health awareness program, focusing the public's attention directly on the pharmacist as a health care resource. "Consult your pharmacist" was the theme of APhA's recent telephone hot line with *USA Today*, both the newspaper and the television program. The enclosed reprints illustrate how we are telling the American public about the services you provide.

"Rx Healthline: A Word from Your Pharmacist" is another product of APhA's expanded outreach efforts to the consumer. The first supplement was included in the September *Cosmopolitan*; the second, a completely new edition, will be in the November *Redbook*. A copy is enclosed for your review. You may have additional copies, at a nominal fee, for distribution through your pharmacy. It has been estimated that we will reach 50 million Americans through this program by year's end.

APhA is working for you, providing you with practical, useful information to share with your patients; striving to create an environment in which American consumers are truly comfortable consulting with their pharmacist about prescription and nonprescription drug products.

This mailing is being sent to over 120,000 pharmacists nationwide — APhA members and nonmembers alike. I have enclosed an APhA membership enrollment postcard. If you are already a member, I would appreciate your giving this postcard to a pharmacist colleague who does not hold current membership. In the event you are not a member, I ask that you give membership a try by using the enclosed postcard. We need your help. These programs require huge resources, and APhA receives the majority of its revenues from membership dues.

These are exciting times and I need you to be a part of them. With your help we can do even more for the advancement of the profession of pharmacy as an essential element in providing health care for Americans. Let me hear from you, and let APhA begin serving you.

Sincerely,

John A. Gans, PharmD
Executive Vice-President

P.S. To join APhA immediately, or to order additional copies of "Rx Healthline: A Word from Your Pharmacist," call 1-800-237-2762.

Enclosures: Generic Drug Fact Sheet: For the Pharmacist
Generic Drug Fact Sheet: For the Patient
Pharmacy Today
USA Today reprint
Rx Healthline
APhA Enrollment Postcard

Generic Drug Fact Sheet: For the Pharmacist

The National Professional
Society of Pharmacists



**American
Pharmaceutical
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APhA

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Dear Pharmacist:

The recent national news stories about fraud in the generic drug industry have raised serious concerns among consumers.

To help you answer some of the questions you may be asked by your patients, the American Pharmaceutical Association (APhA) has prepared this fact sheet.

We've summarized the events surrounding the generic drug controversy and prepared a question-and-answer sheet for consumers, which you may copy and hand out to your patients. A space is provided for your pharmacy name and logo.

We hope this information will prove useful. Should you have any further questions, please feel free to contact Arthur H. Kibbe, APhA director of scientific affairs, at (202) 429-7582.

Major Events in the Generic Drug Scandal

1987 — Mylan Laboratories Inc., hires private detectives to determine why Mylan's applications to the Food and Drug Administration (FDA) for generic drug approval were not being reviewed as quickly as other companies' applications.

July 1988 — Representatives of Rep. John Dingell (D-Mich.) and the Health and Human Services inspector general make an unannounced visit to the FDA, where they interview staff in the Generic Drug Division and seal the office of a division branch chief.

April 1989 — Charges are filed against some FDA employees and representatives of the generic drug industry. The FDA begins inspections of generic drug firms to check for possible violations of the law.

June 1989 — Vitarine Pharmaceuticals is discovered to have substituted the patented drug Dyazide in place of its generic version for analyses to receive FDA approval.

July 1989 — Three FDA employees plead guilty to accepting or giving illegal gratuities; Par Pharmaceutical and its Quad Pharmaceuticals unit plead guilty to making illegal payoffs.

August 1989 — Plans are announced to strengthen the FDA's review procedures for generic drugs. The FDA begins analyzing

samples of the 30 top-selling generic drugs and adds 20 companies to the list of 11 it is inspecting.

Also, the FDA announces that Bolar Pharmaceutical's version of Dyazide is not "of proven therapeutic equivalence to the brand-name drug Dyazide." In a related event, allegations are made that Bolar tried to cheat on bioequivalency tests for its antipsychotic drug thioridazine.

September 1989 — FDA staff testify that 11 of the 13 generics manufacturers inspected so far have problems that require product recalls. These companies had been targeted first because of suspected problems.

A Closer Look at the Problems

At APhA's recent End-of-Summer Science Symposium, FDA Commissioner Frank Young outlined the problems being identified as the FDA investigates generic drug manufacturers. They include:

- **Bioequivalency Studies.** The FDA has evidence that two companies tried to substitute the innovator drug for their generic version during bioequivalency testing. Three firms falsified information on production runs used to support their Abbreviated New Drug Application (ANDA).

- **Stability Data.** Some companies have altered data submitted in support of their ANDAs that were used to establish the product's shelf life or failed to follow the approved study designs.
- **Deviations from Manufacturing Specifications.** Some companies have changed manufacturing processes without informing the FDA; have failed to demonstrate that a product meets specifications after "scaling up" from small batches to full production runs; or have poor or missing records.

Recalls

To date, 29 generic drugs have been recalled by 13 manufacturers as a direct result of FDA investigations. These recalls are all class II: use may cause temporary or reversible medical problems.

To stay informed about the latest recalls pharmacists can refer to the regular listing in APhA's biweekly newsletter *Pharmacy Today*. You can also call the FDA's drug recall coordinator at (301) 295-8054 or the Center for Drugs at (301) 295-8012.

FDA's Plan of Action

As already mentioned, the FDA has begun sampling and analyzing the 30 most prescribed generic drugs and has launched a comprehensive inspection of the 20 leading manufacturers of generic drugs.

Almost 1,100 samples have been checked so far; less than 1% of the products tested do not comply with specifications. Almost 2,000 samples will be analyzed by December 7, 1989.

The FDA's overall strategy for tightening generic drug review procedures includes the following:

- Establishing an independent ombudsman who will report directly to the FDA commissioner and will be responsible for resolving disputes between the FDA and generic drug companies.
- Working closely with the inspector general of Health and Human Services in criminal investigations.
- Helping to develop new legislation to submit to Congress that will allow the FDA to act more promptly against criminal activity related to drug approval applications.
- Increasing the manpower and funding of the FDA's Generic Drug Division to allow for more inspections and closer monitoring of manufacturers.

APhA's Response

Besides monitoring the generic drug issue daily and keeping pharmacists informed through this and other publications, APhA has taken the following actions:

- Sent a letter to FDA Commissioner Frank Young and Rep. John Dingell (D-Mich.) supporting increased resources for

the FDA's Generic Drug Division and offering to help resolve this issue as rapidly as possible. APhA is also working with congressional staff to help develop legislation that strengthens the ANDA process and the FDA's procedures for monitoring generic drug manufacturers.

- Called together a Bioequivalency Task Force of scientists and practitioners to review the current problems and develop materials for pharmacists and patients on the correct use of generic drugs.

What Pharmacists Should Do

How should you, the pharmacist, respond to the generic drug situation?

- As the health care professional most capable of selecting the correct drug product for the patient, you should inform yourself as much as possible about the product, its manufacturer, and its distributor before dispensing it to your patients.
- Stay abreast of the latest news reports involving generic drugs and be prepared to answer patients' questions.
- Check for bioequivalence. Remember that even if products contain the same active ingredients, they are not always bioequivalent because of differences in manufacturing procedures or inert ingredients. The selection of the appropriate product from numerous pharmaceutical products should be based on reliable bioequivalency data and on the therapeutic needs of the patient.

The FDA publishes a reference text called *Approved Drug Products with Therapeutic Equivalence Evaluation*, more commonly called the Orange Book, which rates drugs on their suitability to be substituted for the innovator product.

The FDA's Orange Book uses a two-letter code to designate the status of a multisource product. All products that have a designation beginning with the letter A are considered bioequivalent. Those products with a designation beginning with the letter B are not considered bioequivalent. The second letter of the code designates the type of information the FDA used to determine the product's overall bioequivalency testing.

The FDA's two-letter rating system will help you select an appropriate product for your patient. It's important to note that almost 20% of the drugs listed in the Orange Book are not A rated and should not be substituted.

You should always exercise care when selecting drug products with narrow therapeutic indexes or when selecting products for patients with multiple diseases or severe metabolic disorders. Remember, at times it is as inappropriate to switch from a generic to a brand-name product as it is to switch from a brand-name to a generic product.

Also, when you dispense a refill of a generic product, avoid switching to a product made by a different manufacturer in order to ensure that the patient receives the most consistent therapy.

Generic Drug Fact Sheet: For the Patient

Dear Patient,

Recent news about problems at the Food and Drug Administration (FDA) and fraud by generic drug manufacturers has raised questions about the safety and quality of generic drugs.

As your pharmacist, I hope this information will be of help to you. If you have any questions, please feel free to ask me.

Your Pharmacist

Q What is a generic drug?

A It's a copy of a brand-name drug whose patent has expired. A generic is sold under a common or "generic" name for that drug, not the brand name. For example, the brand name for one well-known tranquilizer is Valium, but it is also available under the generic name diazepam.

Generics often become available for sale shortly after the patent on the brand-name product expires.

Q Who makes generic drugs?

A There are more than 200 manufacturers of generic drugs in the United States. Some companies make only generic drugs. And some generic drugs are made by divisions of major brand-name companies.

Q Why would I take a generic drug instead of a brand-name product?

A Generic drugs are usually less costly than brand-name drugs yet work just as well.

Q Why are generics getting so much attention in the news?

A For one thing, it was recently found that some companies used another company's brand-name drug instead of their own generic drug in tests for FDA approval. As a result, some generic drugs were never properly tested for safety and efficacy.

The products involved in these incidents have been withdrawn from the market.

Also, three FDA chemists who review generic drugs for approval admitted they accepted illegal gifts from generic drug companies to speed up the process for approving their drugs.

Now the FDA has expanded its inspection of generic companies and their products to look for other problems. More than 1,000 products have been tested so far. Of these, 99% show no problems.

Q Are generic drugs as reliable as the brand-name product?

A All drugs sold in the United States must meet strict FDA requirements. A generic drug that can be safely used instead of the brand-name drug gets a special rating.

As your pharmacist, I select only those products I know have met the FDA requirements. I also review the quality of the manufacturers and the availability of the product.

Q How do I know if I'm taking a generic product?

A If you have a question about a specific prescription, please feel free to ask me.

More than a third of the time, pharmacists give patients generic drugs rather than brand-name drugs. This is because generic drugs cost less and save patients money, yet they achieve the same medical results. So it's possible that your prescription is a generic product.

Q How can I be sure my generic drug product is safe?

A If you're concerned about a drug you're already taking, ask me about it. I get bulletins from the FDA and my national pharmacy associations that keep me up-to-date on drug products and recalls.

If there is a serious problem with a drug—either brand-name or generic—I remove it from my pharmacy right away.

If the drug you are taking seems to be working and you have no unexpected side effects, you shouldn't worry. However, if you have side effects or think the drug isn't working as well as it should, consult your physician.

Remember, if you have a prescription medicine that you are supposed to take until it is gone, do not stop taking it without checking with your physician or pharmacist.

Your pharmacist is an information resource. If you have any questions about drugs you're taking, stop in and ask me or call me at:

Please feel free to reproduce the fact sheet on the other side of this page so you can distribute it to your patients. Add your pharmacy name and logo in the space on the reverse side if you wish.

Please put your telephone number
in the box on the reverse side.

Ms. LLOYD. Dr. White, I understand you came all the way from Tennessee to be here this morning. We thank you very much. We would like to hear from you at this point and then have some questions for both of you.

Dr. COBB. Kentucky is not that far off the road, either.

Ms. LLOYD. Did you come on up this morning?

Dr. COBB. Yes, Ma'am.

Ms. LLOYD. I appreciate both of you being here.

**STATEMENT OF CHARLES W. WHITE, M.D., FAMILY PRACTICE
PHYSICIAN, LEXINGTON, TENNESSEE**

Dr. WHITE. Thank you, Madam Chairman, for allowing me to testify. It is deplorable to me and to my profession that some of these fraudulent acts did occur in the drug industry and in the FDA. I agree with that.

You mentioned some of the American Academy's policy related to generic drugs. I really feel strongly that those policies are good policies and should be followed and watched. I don't think there's anything wrong with them.

There are drugs and conditions in which substitution can be made and should be made. I think it's appropriate, and I think it can lead to cost savings for patients.

I do think that the patients themselves have to do some shopping around at drug stores. I think in some instances the savings are not passed on to the patients, or possibly.

In Tennessee I serve on the Medicaid formulator committee for Tennessee. In Tennessee, when a new drug or when a drug goes off-patent or loses its patent, we submit the manufacturer's drugs to a department of pharmacy at the University of Tennessee. They go through the bioavailability and bioequivalency of these drugs and determine whether or not they are bioavailable and bioequivalent.

When they are approved, they are added to our Medicaid formulator list. We sometimes do not add drugs that the FDA actually approves, so that we think our standards may be a little bit better than the FDA.

Ms. LLOYD. We do our own testing, don't we, in the State of Tennessee?

Dr. WHITE. Yes. For new drugs that come on the formulary new, we do. Now older drugs have either been tested or are grandfathered in.

Ms. LLOYD. Where do we do that?

Dr. WHITE. The University of Tennessee. The lab is Dr. Marvin Myers' lab. He's a well-respected pharmacologist across the United States.

Ms. LLOYD. In Knoxville?

Dr. WHITE. No, it's in Memphis.

Ms. LLOYD. In Memphis? The Memphis school. Thank you.

Dr. WHITE. The FDA does use a 20 percent availability rule which means that a drug can be plus or minus 20 percent available. Personally, I think this is a little too liberal. I would like for it to be maybe 10 percent available, plus or minus 10 percent. I think that figure is a little too liberal.

I think that the generic drug industry—in summary, I think there's a place for generic drugs. I just don't think that we ought, as physicians, that we ought to blanket substitute every drug as a generic drug if it's available. I also don't think we ought to give a blanket approval to all generic drugs. I think this should be individualized for the patient and should be done between the patient and his physician with the cooperation and trust of the pharmacist.

[The prepared statement of Dr. White follows:]

CHARLES W. WHITE, M.D.
14 Hospital Drive
Lexington, Tennessee 38351

February 23, 1990

Chairwoman Lloyd, members of the Sub-Committee on Housing and Consumer Interests of the Select Committee on Aging.

I want to personally thank you for allowing me to testify about this most important matter related to consumer affairs. It is deplorable to my profession and to me personally that any fraudulent acts have been perpetrated by members of the generic drug industry or the employees of the Food and Drug Administration. I believe that there have been some misleading reports in the press regarding generic drugs in general and that there are some quality generic drugs available to the general public.

As a physician, I am continually concerned that my patients receive the best drugs that are available to them at the most economical price. There are patients in whom generic drug substitution should be done very carefully - for instance, those elderly patients above 75 and living alone. There are diseases such as diabetes, cardiac problems, and mental problems which should be monitored very carefully if any substitution of generic products is made; and there are a few drugs such as loop diuretics which should not be substituted. Lastly, there are many drugs, conditions, and situations in which the substitution of generic drugs will not endanger the patient, and in

these situations will lead to considerable savings to the patient.

I have served on the Medicaid Formulary Advisory Committee for the Department of Health and Environment in the state of Tennessee since 1983. During this time I have become familiar with the process used in our state to allow generic drug substitution. In addition to FDA approval, many - if not all - generic drugs are submitted to the University of Tennessee Department of Pharmacy for testing related to bioavailability and bioequivalency. If the drugs which are submitted are not considered bioavailable or bioequivalent by these standards, they are not added to the Medicaid Formulary. If added to the Medicaid Formulary, they are considered to be substitutable and safe for public consumption. In Tennessee if a generic drug is added to the Medicaid Formulary, pharmacists and physicians across the state may consider this to be a safe drug for substitution and to be an effective drug with which to treat the patient. At the present time, the FDA uses a 20 percent rule related to generic drugs. Of course, this means that a product may be plus or minus 20 percent of the availability of a brand name product. I personally consider this to be far too liberal, and would hope that in the future the FDA would consider changing this to plus or minus 10 percent of the availability of the brand name product.

In summary, I believe that there is a place for generic drugs. I believe there can be cost savings which can be passed on to the patient by the use of generic drugs, but I do not believe that every patient and every illness should be treated with generic drugs.

Thank you very much.

Charles W. White, M.D.

CWW:pf

Ms. LLOYD. Do you agree with that, Dr. Cobb?

Dr. COBB. Most certainly.

Ms. LLOYD. I want to ask both of you the same question here. Would you describe for the Subcommittee what you think would be a good, healthy interaction between the patient and a pharmacy or the pharmacist, and between the patient and the physician, when it comes to the process of prescribing drugs?

Dr. WHITE. Well, I think we heard earlier that patients and people who use physicians have had problems with communication. I personally think there should be open lines of communication between the patient and the physician.

As a physician, I see open lines in my town all of the time between physicians and pharmacists. We talk about people who are drug abusers. We talk about patients' drugs and whether or not they would qualify to be a generic recipient. We talk about all kinds of things like substitutions, et cetera. I see good, open lines of communications between physicians and pharmacists.

I personally recommend good, open lines of communication with your physician. If you don't have that, then perhaps you need a physician with whom you can communicate.

Ms. LLOYD. Dr. Cobb?

Dr. COBB. Communication is the key. I must point out from some of the earlier testimony about leaflets. It's an excellent communicative tool. It revisits the subject of approximately 10 years ago of a bill before this Congress called PPIs, patient package inserts. It was to be an insert that was to go with every drug in America to every patient. The legislation failed. I believe that pharmacy was against it and medicine was against it. Just the sheer volume was one problem. We were going to have to build a building to house the pieces of paper. Physicians, hospitals were not exempt. In addition to that, the problem of side effects—if I say to this group, "Take this drug. You're probably going to have a headache," you probably will have a headache whether the drug caused it or not.

We really get into some problems with too much information. Now some consumers know how to handle it; other consumers do not. What we have to do is individualize our communication between patient and pharmacist, patient and physician. If we can do that, we'll solve this problem. We're, organized pharmacy, is trying. It is difficult.

Ms. LLOYD. The little stickers on bottles ought to do some good, shouldn't they?

Dr. COBB. Yes. Computers have helped greatly because now computers can not only generate stickers, but bigger pieces of paper by the printer. It's stored in there. We don't have to store the paper. We just store blank paper and it prints out what we want. That's a step in that direction.

Ms. LLOYD. I want to go back to the comment of the first panel that we had, that they had a problem with some of the interaction between some of their medicines. They say that pharmacists sometimes are not allowed to give out this information. It seems to me that, if they go to two or three different doctors and two or three different pharmacists, then that is the responsibility of the patient.

Dr. COBB. Let me introduce Dr. Art Kibbe, who is our scientific director, and let him comment on that.

Dr. KIBBE. The practice of pharmacy governed by the individual State boards of pharmacy in the United States do not prevent pharmacists from counseling. In fact, in at least 28 States they are required by the practice acts under which they practice to give advice sufficient for the patient to be able to use the medication appropriately. I think, although there might be a few instances of some pharmacists who didn't want to give advice to that individual patient, that's not the common practice, nor should it be considered the standard practice. The American Pharmaceutical Association, in conjunction with the American Association of Colleges of Pharmacy, has over the years continually updated what we call the standards of practice of pharmacy, and included in it is the essence of our practice, communication, so that patients use drugs appropriately.

We select from those drugs available drugs which are equivalent, so that we maintain a good, tight cost control and the patient gets optimum therapy.

Ms. LLOYD. On the computer screen, you can call up all the drugs that the patient is taking and advise them if there would be problems combining?

Dr. COBB. One of the problems there lies with patients who do not—some patients jump from physician to physician for a lot of reasons, but generally I think most Americans have a physician, a family physician. Unfortunately, sometimes they do not view the pharmacy in the same way. We obviously cannot check drug interactions if a prescription is filled at another pharmacy, jumping from pharmacy to pharmacy. That is another communication problem between us and consumers.

This committee can help get the word out: we need consumers to select a pharmacy just like they select their physician. If the pharmacist has a poor bedside manner—I realize it's not the bedside—I'd hope they'd get rid of that pharmacist and get another one, the same way they do physicians. We always talk about their bedside manner. We need to communicate better with patients about that.

If filled in one pharmacy and if computerized, yes, we could certainly—we don't need to be computerized. Drug reactions are easy to check for.

Ms. LLOYD. I really appreciate the input of you two gentlemen. I want to really apologize to you for giving you the short end of this hearing today, because I do appreciate your being here. We will be submitting some questions in writing to you that we'd like for you to respond. I want to thank everyone in the audience, everyone that's participated, our reporter, the staff.

I think it's worth saying that, by and large, everyone who's testified here today certainly has the well-being and concern of our seniors at heart. Granted, there are a few out there that are greedy, that really aren't the people they should be, and they're getting brushed over with the same brush, and it's tragic. At the same time, that gives us more concern to really police those persons. It's certainly a breach of trust of the American people.

If there are no further comments, then the Subcommittee stands adjourned.

[Whereupon, at 12:01 p.m., the hearing was adjourned.]

APPENDIX I

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**American Heart
Association**

Office of
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*Dedicated to the reduction of disability
and death from cardiovascular diseases
and stroke*

March 14, 1990

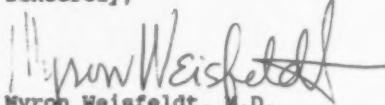
The Honorable Marilyn Lloyd
Chairman
Housing and Consumer Interest
Subcommittee
House Select Committee on Aging
717 House Annex 1
Washington, D.C. 20515

Dear Chairman:

The American Heart Association (AHA) would like to submit the enclosed statement to the Housing and Consumer Interests Subcommittee for the record on the need for restoring public confidence in the generic drug industry.

Thank you for your consideration of our comments.

Sincerely,


Myron Weisfeldt, M.D.
President

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*Dedicated to the reduction of disability
and death from cardiovascular diseases
and stroke.*

American Heart Association

Statement on Generic Drugs

Submitted to the Housing and Consumer Interests Subcommittee of the House Select Committee on Aging

**The Honorable Marilyn Lloyd
Chairman**

March 13, 1990

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The American Heart Association (AHA) appreciates the opportunity to submit testimony to the Subcommittee on Housing and Consumer Interests on the issue of generic drugs. We commend Chairman Lloyd for her leadership in focusing on the need of restoring public confidence in the generic drug industry. AHA would like to work with the Subcommittee to enhance the speed and breadth in developing legislation and other measures to strengthen the FDA generic drug product approval and compliance processes and to restore public confidence in generic drug products.

The AHA is a voluntary nonprofit organization funded by private contributions. Our mission is to reduce disability and death from cardiovascular diseases and stroke. Despite progress in research, in 1987 heart and blood pressure diseases killed nearly one million Americans, almost as many as cancer, accidents, pneumonia, influenza, and all other causes of death combined. High blood pressure killed 31,000 Americans in 1987. An estimated 61 million Americans aged six and older have high blood pressure. Because medical science does not understand the causes of most cases of high blood pressure, it is hard to say how to prevent it. Generally speaking, the older people get, the more likely they are to develop high blood pressure. When high blood pressure exists with obesity, smoking, high blood cholesterol levels or diabetes, the risk of heart attack or stroke increases several times. Age is one factor that cannot be changed. Eating a proper diet, losing weight, restricting salt (sodium) intake and following a program of medication all may be prescribed to lower blood pressure and keep it within healthy limits. In addition, black Americans have an almost one third greater chance of having high blood pressure as compared to whites, and because

this segment of the population tends to be poorer and less economically advantaged, it becomes critical that lower priced drugs be made available to them.

Many in industry, Congress and the Federal government, including the FDA, trace the roots of the generic drug scandal to a multitude of factors, including the short implementation period for the Drug Price Competition and Patent Term Restoration Act of 1984, the deluge of Abbreviated New Drug Application's (ANDA) since the passage of the Act, the absence of regulations to implement the ANDA title of the Act, the intense desire of generic drug manufacturers to gain the economic advantage of being first to gain approval of a drug, coupled with a dwindling FDA staff and budget.

A major goal of the 1984 law was to facilitate the entry into the marketplace of generic versions of pioneer drugs whose patents had expired. FDA cites a marked increase in the number of ANDAs since the law's enactment - 1,069 new applications in fiscal year 1985, compared with 470 in FY 1984.

Generic drug products have evolved into a \$3.5 billion business, saving Americans millions of dollars and helping to control our Nation's escalating medical costs. These products are vitally important in the area of cardiovascular disease, especially diuretics, beta blockers and vasodilators for hypertension; digitalis diuretics and vasodilators for heart failure; and beta blockers, nitrates, and calcium channel blockers for chronic coronary artery disease. Generics provide a low cost, but effective method of treatment for over 60 million hypertensive Americans who could require medication.

The enactment of Public Law 98-417, the Drug Price Competition and Patent Term Restoration Act of 1984 on September 24, 1984 led to the proliferation of generic drugs on the market. However, the deluge of Abbreviated New Drug Applications (ANDA) at the Food and Drug Administration (FDA), coupled with the overwhelming desire to achieve millions of dollars in profits and gain market share being granted the first approval of specific generic drug products, may have caused several generic drug manufacturers to offer bribes to selected Food and Drug Administration (FDA) officials and to participate in "unsafe, improper, and illegal practices," such as irregularities in materials submissions, falsification of information, inept record keeping, incorrect manufacturing data, and infringement of Current Good Manufacturing regulations.

Generic diuretics and anti-hypertensive drugs have been hard hit during the progression of the generic drug scandal. Upon discovering that they had used the brand name drug Dyazide for testing, Vitarine recalled its triamterene 50 mg. and hydrochlorothiazide 25 mg. capsules. On November 20, 1989, FDA issued a proposal to withdraw approval of Bolar's generic version of Dyazide. FDA had earlier reclassified this Bolar product from "AB to BX," stating that its version is not of "proven therapeutic equivalence to the brand name drug Dyazide." According to FDA, "withdrawal of Bolar's product would leave no generic version of the brand name on the market." In addition, Par Pharmaceutical voluntarily recalled its generic triamterene and hydrochlorothiazide tablets, marketed as a replacement for Maxzide, a diuretic and anti-hypertensive. The recall was made after the company learned that batch samples had been substituted during an FDA inspection. On October 29, 1989, FDA announced a recall of several drugs

manufactured by Quantum Pharmics because "the size of the production run submitted for testing to gain FDA approval was in each case misrepresented as much larger than it actually was." An anti-hypertensive drug, minoxidil, was among them.

While these scandals and problems made front page news across the country, the FDA's analysis of the 30 top-selling generic drugs revealed that only 1.1 percent of the test sampled did not meet quality standards. These tests, similar to earlier survey results of generic and brand-name drugs, lead then FDA Commissioner Young to answer his own question before Congress on November 17, 1989 that "are the generic drugs on the market safe and effective? The answer appears to be a qualified yes.... but our job is not done, though and we will keep that qualification until we are done."

Despite Young's pronouncement, the generic drug scandal has shaken the Nation's confidence in these products. According to Young's congressional testimony on November 17th, "...misconduct exhibited by certain individuals and companies in the generic drugs industry...have tarnished the integrity of the industry, caused upheaval in our drug review system, and created doubts in the minds of many who prescribe, dispense, and use generic drugs."

In October 1989, a Gallup survey commissioned by Lederle Laboratories shows that while 77 percent of 1,009 households using generic drugs said their confidence in these products had been rocked, only nine percent changed back to brand names. Specifically, the survey revealed that 66 percent are very satisfied with generic drugs, 25 percent are fairly satisfied, and 51 percent think quality

control for generic drug products is not as good as that for brand names. According to the survey, women, the highly educated and the wealthy, were more likely to change their minds about generic drug products after learning about the scandal. Approximately, 50 percent generated adverse attitudes about both generic and brand-name industries.

Most people dependent on generic drugs are concerned with the quality of drugs. However, people with limited resources must be able to obtain medication and not be deprived of the generic version.

Under the Administration's budget proposal \$45 million is requested to assure the continued safety of human generic drugs. This will provide the highest level of generic drug activity since 1984. With the additional resources requested, FDA will be able to: increase the review of generic drug applications, establish a separate office of generic drugs, reexamine a substantial portion of the 2,000 generic drugs approved since passage of the Generic Drug Act of 1984, increase the number of generic drug samples collected, and increase the frequency with which generic drug plants are inspected. Expanded surveillance efforts have been underway for the past six months and the supplemental funds would be used to meet these increased operational expenses. A supplemental budget request for \$14 million is proposed for FY 1990.

As the FDA and Congress continue to work towards strengthening the generic drug product approval and compliance processes, the restoration of public confidence in these products is essential. According to Diane Colasanto, vice-president of the Gallup Organization in Princeton, New Jersey, the "key in the

process of restoring confidence are pharmacists. They should communicate their feelings about generics and manufacturing practices to consumers." The American Heart Association's Office of Public Affairs (OPA) has therefore initiated a contact at the American Pharmaceutical Association (APhA). We have also alerted our Affiliates nationwide to use their contacts and community based organizations to work with physicians, pharmacists and others in restoring public confidence to the generic drug industry. Recently, APhA sent fact sheets to over 120,000 pharmacists nationwide. The mailing included separate generic drug fact sheets for the pharmacist, and one for the pharmacists to distribute to patients. We commend the APhA for acting quickly and responsibly in their efforts.

The AHA pledges to work cooperatively not only with the Housing and Consumer Interests Subcommittee, but also with the Oversight and Investigations Subcommittee chaired by Representative John Dingell. We believe that the health and welfare of the American population depends in part upon a strong, viable, and reliable generic drugs industry. Our goal should be restoration of 100% public confidence, coupled with the necessary regulatory process to ensure safety and efficacy.

We thank the Subcommittee for this opportunity to provide comments on the engendered skepticism about the quality of generic drugs. We would like to continue to assist the Subcommittee in its efforts to restore confidence the American people once had in the industry. Thank you for your careful consideration of our comments.

Statement for the Record
Office of Inspector General
Department of Health and Human Services
for the
Subcommittee on Housing and Consumer Interests
Select Committee on Aging
on
Developments in the Generic Drug Industry

March 1, 1990

This Statement for the Record summarizes the role of the Office of Inspector General, Department of Health and Human Services in the recent generic drug investigations, the general status of those investigations, and the findings of our report on the Food and Drug Administration (FDA) generic drug approval process.

Before elaborating on our role in the generic drug investigations, we would like to present some background on our office. Statutorily created in 1976, the mission of the Office of Inspector General (OIG) is to root out fraud, waste and abuse in the Department's programs. Although part of the Department, the office is to be objective and independent and report both to the Secretary and the Congress on ways to make the Department's programs more efficient and economical.

In this capacity, our audit, inspections and investigations offices have responsibility to oversee all the programs within the Department including those under the Food and Drug Administration.

Last year, our office generated over \$5.5 billion in savings, fines, restitutions and recoveries, and assisted in the prosecution of over 1,200 criminal and civil cases. Until 1989, the number of FDA related criminal convictions and civil cases averaged 15 to 20 cases annually. FDA related cases were not a major part of our investigative workload.

In June 1988, the Subcommittee on Oversight and Investigations of the House Committee on Energy and Commerce referred to the OIG allegations of misconduct in the Generic Drug Division of the FDA. The information alleged (1) possible acceptance of gratuities from pharmaceutical companies by employees of the generic drug division, (2) potential fraudulent statements in applications for approval to market drugs, and (3) possible drug substitution in the course of the approval process. The FDA Commissioner concurred with the Subcommittee's position that the Department's investigation of these charges should be conducted by the OIG.

The OIG's investigation of FDA's internal policies and operations was brought to the attention of the United States Attorney for the District of Maryland, under whose auspices this investigation proceeded to prosecution. It is standard practice for OIG criminal investigators to refer the matter indicating a violation of Federal Law directly to the Offices of the United States Attorneys for immediate actions.

The OIG investigation of referred cases resulted in 8 successful prosecutions - 3 FDA employees, 3 generic drug companies employees and 2 drug companies. To date, our investigations have led to the convictions of:

- o Charles Chang, a supervisory chemist in the Division of Generic Drugs (FDA), who pled guilty to a racketeering charge in connection with his acceptance of illegal gratuities from a generic drug company representative. He was subsequently sentenced to 1 year incarceration in a work release program, and 3 years probation, and was ordered to pay a \$10,000 fine and to perform 1,000 hours community service. In addition, he resigned his position at FDA.
- o David Brancato, a chemist who worked for Chang in the same division. He also pled guilty to accepting illegal gratuities from a generic drug company representative. He was subsequently sentenced to 30 days incarceration in a work release program, and 3 years probation, and ordered to pay a \$3,000 fine and to perform 500 hours of community service. He has also resigned from FDA.
- o Walter Kletch, also a chemist in the Generic Drugs Division, who pled guilty to accepting illegal gratuities from a generic drug company representative. He was subsequently sentenced to 30 days incarceration in a work release program, and one year probation, and was ordered to pay a \$1,000 fine and to perform 120 hours of community service. He is no longer with FDA.
- o Ashok Patel, the president of Par Pharmaceuticals, Inc., a generic drug company, who has pled guilty to paying illegal gratuities. He was sentenced to 30 days incarceration in a work release program, and 18 months probation and was ordered to pay a \$150,000 fine.

- o Dilip Shah, the president of Quad Pharmaceuticals, Inc., also a generic drug company. Mr. Shah was found guilty of paying illegal gratuities and was subsequently sentenced to 60 days incarceration in a work release program, 2 years probation, and 1 year community service and was ordered to pay a \$250,000 fine.
- o Raj Matkari, the president of the generic drug company, Pharmaceuticals Basics, Inc., who pled guilty to paying illegal gratuities. He was sentenced to 3 years probation, and 500 hours of community service and was ordered to pay a fine of \$2,000.
- o Par Pharmaceuticals, Inc., a corporate entity, which entered a guilty plea based on the actions of its corporate officer, Ashok Patel. The corporation was required to pay \$150,000 fine.
- o Quad Pharmaceuticals, as a corporate entity, which also entered a guilty plea based on the actions of its president, Dilip Shah. The corporation paid a \$250,000 fine.

From our investigative perspective, we believe that investigation of the FDA generic drug division has been successful. However, more needs to be done. Through our efforts and those of FDA officials, we have targeted for further investigation at least three generic drug companies who appeared to have obtained approval for generic drugs based on fraudulent applications submitted to the FDA. As a result of the FDA and OIG work and through voluntary efforts by generic drug companies, numerous products have been recalled from the market. Further, even though the bulk of our FDA caseload has been transferred to the

Department of Justice for further action, we anticipate

additional criminal charges to be filed in both the corruption (payoffs to government officials) and fraud (product substitutions) aspects of these investigations.

In addition to our investigative responsibilities, we have also performed other reviews of the generic drug activities of FDA as well as of studies of drug utilization by the elderly.

In April 1989, we issued a report on Medicare Drug Utilization Review, which was designed to provide a better understanding of the major problems and needs that a Drug Utilization Review (DUR) program should address.

We initiated this study because at that time, Congress was debating the Medicare Catastrophic Coverage Act of 1988, and part of that legislation mandated the Department to design and operate a Multi-level DUR effort to improve quality of care, avoid unnecessary Medicare and personal expenditures and maintain program integrity.

Some of our findings showed that:

- o there is a wide spread problem of mismedication among older adults;

- o the problem of misedication among the elderly reflects a series of systemic weaknesses throughout the drug therapy delivery system:
- o although Americans age 60 and over comprise only 17 percent of the total U.S. population, they account for 39 percent of all hospitalizations and 51 percent of deaths from drug reactions; and
- o in 1987, at least 200,00 older adults were hospitalized due to adverse drug reactions, or experienced an adverse drug reaction while hospitalized.

Then in September 1989, the OIG issued a report entitled: "Vulnerabilities in the Food and Drug Administration's Generic Drug Approval Process".

Our review was performed as a result of the vulnerabilities identified by our investigation of fraud and corruption within the generic drug approval process. Further, the Commissioner requested that we identify and recommend corrective action for the weaknesses and vulnerabilities in the system which gave rise to these problems and allowed preferential or detrimental treatment to be given to certain drug manufacturing firms.

We determined that FDA (1) arbitrarily assigned and reassigned

drug applications to reviewers based on the reviewers' experience with the drug, (2) lacked adequate guidelines to ensure the consistent review of applications, and (3) needed a quality control system to ensure that applications are properly reviewed and that generic drug firms receive equitable treatment. These irregularities amount to a material internal control weaknesses in the generic drug review process that allowed preferential treatment to drug firms. These internal control weaknesses (1) significantly impair FDA's mission of assuring a fair generic drug review process, (2) allow employees involved in the process to violate in the Department's standards of conduct, (3) could deprive the public of competitively priced drugs, and (4) merit the attention of senior officials. Any one of these four effects fits the criteria for a material internal control weakness as included in Office of Management and Budget instructions to agencies for implementing provisions of the Federal Managers Financial Integrity Act of 1982 (FMFIA). As a result of our audit and investigative work at FDA, the Secretary eventually identified the generic drug process a material weakness under FMFIA.

The FDA has yet to evaluate its generic drug review process as is required by the FMFIA and implementing instructions. The Office of Management and Budget requires Federal agencies to segment their operations into internal control areas, perform risk assessments, and perform internal control review of areas with

moderate to high risk, and to correct weaknesses identified. Had it conducted the required internal control review of the generic drug approval process, the FDA might have identified and corrected internal control weaknesses that allowed these irregularities to occur.

In our report, we recommended that the Secretary direct FDA to improve internal controls over the generic drug review process by:

- o requiring branch chiefs to monitor and report to the division director on the progress of Abbreviated New Drug Approval Process (ANDA) reviews;
- o developing policies and procedures for the random assignment of ANDA's to reviewing chemists, or for other appropriate methods for reducing the opportunity to show any partiality to applicants;
- o requiring each request for ANDA reassignment to another chemist, after the initial assignment, be approved and justifications included in the ANDA file;
- o ensuring that reasons for reviewing and approving an ANDA out of sequence from the order it was received are properly documented in the ANDA file;
- o developing policies and procedures for use by supervisory and review chemists to ensure the consistent, comprehensive review of applications;
- o requiring drug firms to submit bioequivalency samples with the ANDA and validating the authenticity of the samples submitted;
- o establishing a quality control review system which includes uniform standards for the review of generic drug applications and operating guidelines for the generic drug application review process; and
- o disclosing in reports required by the FMFIA that there is a material weakness in the internal control structure for the generic drug approval process that allowed preferential treatment to drug firms, and monitoring corrective action

until the weakness is resolved;

We are now finalizing other reports related to the major FDA divisions: innovator and generic drugs, new medical devices and the 510K process for approval. In addition, we have transferred a number of related cases to the Department of Justice.

In the future, some of our FDA related work will focus on abuse of steroids by youth. We want to see if we can understand the nature of the problem and determine why its use is moving so fast in our society. In addition, a special project will focus on the illegal sale and purchase of steroids to create a coordinated crackdown on this problem.

Another activity will review the use of covered outpatient drugs by Medicare beneficiaries, from the standpoint of medical necessity and the potential for adverse drug reactions.

We are continuing our reviews in the FDA area, to ensure that we avoid the kind of scandal that befell FDA's generic drug division. Finally, we will continue our criminal investigations in the FDA to look for that small number of persons who every year commit some criminal fraud against FDA programs.

In conclusion, we would like to point out that the FDA has a unique regulatory responsibility to protect the American consumer. FDA's efforts are designed to ensure public confidence

in the foods they eat, in the drugs they take and in the medical devices they use. The failure of these efforts can adversely impact in many ways both the other programs of this Department as well as the persons who rely upon them.

This concludes our Statement for the Record.



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Memorandum

February 28, 1990

TO : House Select Committee on Aging
Subcommittee on Housing/Consumer Interests
Attention: Honorable Marilyn Lloyd

FROM : Blanchard Randall IV BR IV
Analyst in Social Sciences
Science Policy Research Division

SUBJECT : Generic Drug Hearing Brief

In response to your request for a hearing brief on generic drugs, we are providing the enclosed per your instructions and our subsequent phone conversations.

If we may be of further assistance, please do not hesitate to call (707-7046).

BRIV(JB)kch

GENERIC DRUGS CONSUMER AND INDUSTRY PERSPECTIVES

INTRODUCTION

The U.S. pharmaceutical industry dominates the globe in both production and sales of medicinal health care products. American consumers alone spend over \$40 billion annually on drug products; nearly one-third of the entire world market. The industry is heavily depended upon to treat and/or cure human disorders in an attempt to improve the quality of life. This briefing paper provides some comparisons between brand-name prescription drug products and their generic counterparts, and the campaign these two industry rivals have waged over the decades to convince consumers that their products are superior.

Most consumers think of a prescription drug in terms of its brand-name --a name devised to command attention, be remembered, and importantly, be easily written for prescribing purposes. Generic drugs are chemical equivalents of their brand-name forebearers and, likewise, are sold under chemically descriptive names--names neither pronounced nor written easily. Generic drugs are usually less expensive to purchase if the wholesale cost differential between the brand-name and the generic equivalent is passed on by the pharmacist to the consumer at the point of retail sale. Many have questioned whether or not generic drugs are equally as safe and effective as the brand-name products they imitate. Others have asked if the price differential alone is enough to justify purchasing generics in place of brand-name drugs when that option presents itself, as it so often does today.

MARKETPLACE UNCERTAINTY

The U.S. pharmaceutical industry is highly competitive and diversified; no one company or its products dominate the marketplace. For decades, manufacturers of brand-name drugs have invested vast resources to fund the necessary research and development to discover and market products which they hope will become profitable. New drug discoveries, protected by patent law, may experience years of market exclusivity with little or no direct competition. This short lived monopoly begins to erode when competing drug firms introduce their similar, but slightly modified, formulas into the same therapeutic category, consequently providing physicians with alternative treatment choices. Drugs, which can alter the course of a disease through different metabolic activity, may be introduced, further crowding the field of drugs available to treat a particular disease. However, competition between these alternatives is not as significant as when their respective patents expire and the makers of generic compounds are "free" to market copies of the original pioneer product. For the most part, the generic drug companies are not burdened with the same financial risks as the brand-name industry. They are not required to do the same extensive original research (usually it has already been done by a brand-name company). FDA review for approval should consume less time, and marketing overhead can be less costly.

GENERIC-BRAND NAME CONTROVERSY

Producers of brand-name drugs, often called innovator or pioneer companies, spend enormous sums of money to discover and bring new products to the marketplace. In today's financial climate, it is estimated to cost

approximately \$125 million to bring a new chemical entity to the therapeutic marketplace (practice of medicine). Very expensive preclinical (animal) studies and human trials are required by law to generate the necessary data to prove that a drug is both safe and effective for its intended use. Drug companies must also invest their resources in testing promising compounds that may never become a marketable or profitable product to promote innovation. New drugs that eventually meet the stringent safety and efficacy requirements, and are approved for sale by the Food and Drug Administration (FDA), are protected from imitation by patents. U.S. patents protect innovative products for a period of seventeen years. It should be noted that most pharmaceutical companies file for patents during the early stages of their drug's development, and, as a result, valuable market protection often erodes before a product is even approved for sale.

When a drug patent expires, the original pioneer manufacturer will, in time, be faced with direct competition from generic manufacturers who wish to capitalize on a proven niche of sustained profitability. Generic drug manufacturers must have FDA approval before they can market their products, and it is at this juncture that conflict originates. Although generic drug products have been available for over forty years, opponents of their use have argued that generics are not manufactured and approved in the same manner as their brand-name counterparts.

One of the major debates about using or substituting generics in place of brand-names revolves around whether they are biological equivalents, more than if they are chemical equivalents. Chemical equivalents contain

essentially identical amounts of the same active ingredients. Biological equivalents are drugs that, when administered in the same dose, will provide the same physiological activity to the body tissue. Brand-name drug makers have claimed for decades that many generic drugs often lack necessary biological equivalence, and as a result, do not offer the patient a truly identical, safe, and efficacious form of drug therapy.

Are such charges ever supported through scientific comparisons between competing generic and brand-name products? The answer is a qualified yes. One of the earliest discovered antibiotics, oxytetracycline, was sold for years under the brand-name Terramycin. Terramycin's patent expired in 1967 and numerous generic manufacturers began producing oxytetracycline. The maker of the brand-name drug asked that a comparative evaluation be done to determine if the generic versions produced the same biological activity in patients as did Terramycin. The FDA certified the chemical formulation of each drug (both branded and generic). Subsequent examination determined that patients receiving some generic versions had unacceptably low concentrations of oxytetracycline while others had blood levels equal to those produced by Terramycin. Makers of the generic oxytetracycline (that failed the bioequivalence test) had no choice but to withdraw their products in compliance with FDA's order.

This type of head to head comparison does not typify and indict all generic manufacturers and their products, and with qualified exceptions (over decades), it has not. Nevertheless, when biochemical and bioequivalence inequalities are discovered among competing drugs, pharmaceutical companies

in some cases, have taken advantage of the opportunity to claim medical superiority of their product.

PRODUCT SUBSTITUTION COMES OF AGE

Pharmaceutical innovation moved very rapidly from the 1950s into the 1970s. New drugs were developed, but more often, improvements made on "older" products became more commonplace. As patents on brand-name drugs expired, the generic pharmaceutical industry continued to grow adding more and more competing product alternatives to an already proliferating marketplace. These events, among others, placed new responsibilities on the shoulders of both physicians and pharmacists, as pressures mounted to prescribe and dispense medications with some thought given to consumer health care costs. The enactment of new Federal and State health programs such as Medicare and Medicaid required, where possible, payment or reimbursement for the lowest drug price available.

State antisubstitution laws were some of the first obstacles that stood in the way of wider acceptance of generic drugs. During the post-World War II era, a number of manufacturers began producing "counterfeit" drugs: products similar in size, shape, and sometimes packaging, of brand-names. To quell this trend, States passed laws prohibiting pharmacists from dispensing any product other than the one written (mostly brand-name) by the physician. These laws were a boon for the brand-name producers, who not only considered counterfeits illegal, but of dubious quality as well.

In 1976, the Federal Trade Commission (FTC) began an investigation into the sale of "multisource" prescription drugs with the intent of discovering

whether or not price competition among multisource prescription drugs had been obstructed by state antisubstitution laws. The FTC issued its report three years later and concluded that indeed, "antisubstitution laws impose substantial unwarranted costs on consumers," and that, "repeal of antisubstitution laws would produce significant consumer benefits without compromising the quality of health care." At the time of the report's release, most States were in the process of repealing their antisubstitution statutes, and today, all States, under one scheme or another, permit pharmacists to substitute generic for brand-name products when appropriate.

CONTINUING CONTROVERSY

Although it would seem that market forces, government policy and consumer demands may have firmly established a place for generic products in the evolutionary U.S. health care industry, generic drug producers continue to face difficulties. It is true that, over the years, generics have "captured" an ever increasing percentage of the total prescription drug market, but to accomplish this, they have had to contend with an array of unfavorable court challenges and an ever present atmosphere of resistance from the brand-name drug makers. In the past, generic manufacturers have mounted unsuccessful challenges to FDA's authority which requires approval of their products before marketing. On other fronts, generic drug makers have won the legal right to sell products that resemble the color, size, and shape of their branded equivalents.

Resistance from brand-name manufacturers has been applied in a variety of forms. Brand-name producers have fought to block State legislatures from

repealing ant substitution laws. They have sought court intervention to prevent FDA from publishing therapeutic equivalence lists that were intended to assist States and pharmacies when faced with decisions involving generic substitution. In 1981, the Reagan Administration placed a hold or freeze on the existing practice of approving generics based on already published safety and efficacy data. Congressional oversight hearings on the unannounced policy switch were instrumental in the eventual restoration of the old approval system.

CONGRESSIONAL ACTION

Beginning in the early 1980s, the lobbying organization for the brand-name industry (Pharmaceutical Manufacturers Association) embarked upon a campaign to gain congressional support for a new concept involving increased patent protection for their drug products. The PMA argued that their member companies were not receiving the full benefit of the seventeen-year patent exclusivity established well over a century ago by Congress. The PMA pointed out that drug companies often file for patent protection early in a drug's developmental stages, sometimes years before receiving FDA approval for marketing.

Subsequently, Patent Term Restoration legislation was introduced and immediately drew opposition from the generic drug makers who criticized it as protecting the brand-name pharmaceutical industry. Generic industry supporters claimed that such legislation, if enacted, would, once again, slow their access to the marketplace. Brand-name representatives claimed that passage of new legislation was needed to enhance incentives for future

pharmaceutical innovation. During deliberations on the issue, Congress sought compromise, and eventually enacted what became known as the Drug Price Competition and Patent Term Restoration Act of 1984 (P.L.98-417). In short, the law provides brand-name manufacturers with a "formula" to recoup a portion of "lost" patent life for their products and, at the same time, establishes a statutory mechanism to facilitate a more rapid FDA approval process for drugs no longer eligible for patent protection. Part of the intent of the new law was to create wider competition in the drug market with some expectation that there would be some moderation in the escalation of overall drug prices. Since enactment of the law, hundreds of new generic drug applications have been received by FDA, many have been approved for marketing, but there is little evidence that the law has had a concomitant impact on pharmaceutical prices.

DRUG PRICES

In recent years, drug prices have climbed faster than the overall rate of inflation. In statements to the public and testimony before Congress, pharmaceutical industry representatives have defended the increases as necessary to cover the costs of research and development, marketing, and to produce a reasonable return on their investment. Others believe, however, that this often repeated industry defense is timeworn and that continuous price escalation represents little more than consumer "gouging." Regardless of one's orientation to the debate, the price of a commodity in the U.S. reflects not only the "cost of doing business" but to a great extent "what the market will bear."

Generally speaking, generic drugs can offer substantial savings for consumers, especially if the drug is "multisource," meaning available from more than one manufacturer or supplier. However, just because a drug is multisource does not guarantee that the price differential between a generic and its brand-name equivalent will be passed on to the customer at the point of sale in the pharmacy. It is important to remember that many pharmacies cannot afford to stock all generic equivalents of every brand-name pharmaceutical product. Reportedly, most reputable pharmacies will provide consumers with information about whether or not a physician's prescription can be filled with a less expensive generic drug.

There are circumstances when physicians prefer that their patient receive only a brand-specified product. It is usually the physician's prerogative to determine when a particular patient's medical interests would be better served if only the product written on the prescription was dispensed. Many States provide physicians with a variety of ways to indicate their preference if the choice is not to be made by the patient or pharmacist.

CONSIDERATIONS FOR THE ELDERLY

The rising cost of health care has become a concern of national priority. Although the issue is important to all consumers, it evokes unparalleled levels of distress among the elderly. Older Americans--age 65 and over--comprise the fastest growing segment of the Nation's population. As an age group, the elderly take between 25 and 30 percent of all prescription and over-the-counter(OTC) medications--annual cost expenditures running well into the billions of dollars. Many older citizens are bound or limited to fixed

incomes; paying for their drug costs directly out-of-pocket. This can have a devastating financial impact on someone with a chronic medical condition who needs medication on a continuous basis.

Groups faced with such circumstances will do what is possible to keep costs reasonably within their means. Having access to a safe, effective and reliable source of less expensive drug products contributes to this goal. Through consultation with their doctors and pharmacists, individual consumers can achieve savings by taking advantage of the availability of lower-cost multisource drugs. Under some circumstances, buyer organizations can recognize reduced costs in accordance with high-volume purchasing.

CONTROVERSY REMAINS

The "generic versus brand-name" controversy has remained relatively calm over the past five years. Brand-name makers still take issue with FDA's criterion for approving generic drugs. They argue that FDA's permissible blood-level variances between generic and brand-name products allows generic drug consumers to be at risk of not receiving the therapeutically desired level on active drug ingredients. The FDA contends that their standards for generics and branded drugs are not significantly different; at least, to an extent, that would pose a health risk for consumers. While medical reports surface occasionally that purport health risks associated with certain generic drug products, at the same time generics are prescribed and dispensed in greater volume than ever.

How this prescribing trend will fare in the future remains to be seen. In 1989, U.S. consumers were startled with the unsettling news that some

employees of the FDA generic drug review office had been charged with, and were subsequently convicted of, accepting bribes in exchange for expediting their drug application reviews. Ongoing congressional investigations uncovered evidence that other generic drug companies had been submitting falsified data and bogus drug samples to the agency. As a result of these and other misrepresentations made to government regulators, certain generic producing drug firms actuated product recalls or suspended manufacturing operations altogether. FDA has made a number of drug approval withdrawals and several referrals to the Justice Department for criminal prosecution.

The extent of the problem has not been fully ascertained and awaits further agency and Congressional review. At least one public opinion poll (Gallup) has demonstrated significant consumer awareness of the issue, but to date it is uncertain to what extent users of suspect generic products have been exposed to health risks. In such situations, the FDA recommends that consumers who are taking generic drugs continue to do so, and should they have concerns about their type of medication, consult their physicians or pharmacists.

On November 17, 1989, Dr. Frank Young, former FDA Commissioner testified before Congress that after six months of investigation, the agencies' "findings... present[ed]... a somewhat mixed picture." The agency tested 2,500 samples of the top selling generic drugs, and found that 27, or 1.1 percent did not conform to production quality standards. Following up, the Inspector General of the Department of Health and Human Services, has promised to make recommendations on how the regulatory mechanism can be tightened

and improved to insure that such incidents do not occur in the future. Internal FDA reorganization, or possible law changes mandated by Congress, may still be needed to fully restore confidence in our Nation's supply of pharmaceutical products.

APPENDIX II

Generic Pharmaceutical Industry Association

200 Madison Avenue, Suite 2404
New York, N.Y. 10016
(212) 683-1881

April 24, 1990

Honorable Marilyn Lloyd
U.S. House of Representatives
Select Committee on Aging
Subcommittee on Housing and Consumer Interests
717 House Office Building Annex 1
Washington, D.C. 20515

Dear Congressperson Lloyd:

Enclosed are the answers to the questions you sent along after the hearing.

I think you have already helped allay some of the unwarranted fears about the continued use of generic drugs. One example is this article which went to the AARP membership. One of the major problems with high visibility investigations is to separate fact from fiction. You have begun to do that.

I sincerely hope you pursue this inquiry although I know the problems of "turf". You can eliminate the corruption, establish systems to prevent its reoccurrence and not destroy the competitive pricing of the generic side of the pharmaceutical business. For many older Americans, generics avoid the triage of choosing either medicine or food. As you know so well, that is not a cliché.

Sincerely,

W. F. Haddad

William F. Haddad
Chairman

Answers to Additional Questions:

1. **Question:** Should the public be somewhat suspect of what the FDA says?

Answer: No, I do not think that anyone, including the Congress, needs to be skeptical about FDA as an entity.

I think they can be rightfully concerned about those who corrupted or abused the system and Congress is within its jurisdiction to highlight these faults and in determining if there is a statutory answer to these faults. But FDA's record is too long and too valid for these abuses to create an image that the FDA is not doing its job.

FDA continues to be the final authority of problems from new drugs to AIDs to generics and back again. Within such a large system there are bound to be disagreements, but in evaluating them, observers must be cognizant that many companies and people would like to diminish the FDA authority because it intrudes on their ability to make money. Suffice to say that the FDA is the agency which the rest of the world considers the pace setter, the one to emulate. If a product or a system has FDA approval, that's enough to have it accepted worldwide.

Is the FDA always correct? No. But all things being equal there is no more knowledgeable and impartial authority on pharmaceuticals than the FDA. It would be a tragedy if this current problem caused people to be concerned about FDA's conclusions.

2. **Question:** Do you believe that the bad companies are unable to sell their goods?

Answer: Companies which have been found guilty of corrupting the FDA or the process are now paying a severe penalty in the marketplace. Almost every responsible purchaser, be it buying group or wholesaler, hospital or chain drug store, keeps a scorecard of the so-called "clean" and the so-called "bad" companies and uses it to decide purchases. There are pragmatic as well as ethical reasons behind these decisions. Product insurance is costly and every purchaser must take necessary precautions. Customers

now want to know if the company making the product is suspect or in trouble. Our company, Schein, is a distributor as well as a manufacturer and we know that our customers want to know who makes the products we sell to them and they have informed us they will not purchase products from certain companies. We, in turn, have suspended purchases from certain companies. In addition, the military has prohibited the purchase of products from certain companies and this has always been a barometer in our marketplace.

Some of the companies now in trouble will pay their penalties in the courts and at FDA, hire new personnel and reorganize to FDA's satisfaction, and return to the pharmaceutical business. But before that happens, they will have paid a very high price in terms of both economics and reputation and their return will be slow and expensive.

But there is also a danger here as well. The purchaser, just as others, must make decisions carefully. These decisions must be based on fact not rumor; on actions, not charges. To make these rational, ethical decisions, they need accurate information and must know where to find it. The subcommittee can do a service by advising on where this information can be obtained and to insure that it is quickly available.

3. Question: Do you believe that even the drugs that have been withdrawn by your industry were safe and would have passed the FDA's tests?

Answer: To answer this question accurately, you need to explore why certain brand and generic drugs are removed from the marketplace. Many products are routinely removed from the marketplace for problems not associated with the generic scandal...as my testimony indicated. Most often, it is particular batches produced in a specific time frame that are recalled. These may lack potency, they may have reacted to climatic conditions, they may include unwanted ingredients (some of which may be dangerous) or they may have been mislabelled. Rarely is an entire drug removed from the marketplace, except for exceptional cause, and these are usually products which have been

in the marketplace for shorter periods of time (e.g., Oraflex). When a generic is allowed to compete, the product has been sold for seventeen years and all that needs to be medically known about a product is known. It is also vital to note that there has not been a single generic therapeutic failure. That means, in layman's terms, that no drug which honestly met FDA testing standards has failed.

For the purposes of this answer, I will confine my answer to those drugs which were removed during the last two years or approximately the time frame in which the generic scandal erupted and during which an unusual number of products were tested and manufacturers subjected to intense scrutiny. I will also confine my response to the removal of drugs, not batches.

To date, what does the record show? In one admitted instance, the drug was removed because the brand name was substituted for the generic during the outside laboratory testing process. But FDA concluded the product manufactured and sold was safe and effective, but fraud was involved in its approval. It was removed from the marketplace and the company involved removed almost all its products from the marketplace for re-testing and is now awaiting a decision on which of their products can be allowed back into commerce.

In another well publicized company situation, in two or three as yet unproven instances, something similar is suspected and one product was removed. Eventually, the company recalled most of its products for re-testing. It is not clear what the problems may or may not be with these products or are the results of the re-testing known.

In another instance, a third company removed all of its products from the marketplace and transferred their approvals elsewhere.

In other instances specific products were either downgraded to the "BX" rating or removed, but in most if not all of these situations, the cause was that the paper trail was not provable to FDA's satisfaction (FDA reserves the option to remove these products from the marketplace). In many of these instances, the products are being re-tested.

As the result of the intense FDA inspection many companies were cited for failure to maintain Good Manufacturing Practices; these citations ranged from the closing of a plant (Quantum, Lilly, Abbott) to a regulatory letter (which will effectively prevent FDA approvals of applications (a severe economic hardship) until the condition is remedied to the so-called "483" which is usually corrected within the process and the "EIR" which is a less serious citation. Few, if any companies, emerge from the usual inspections, much less the intense inspection conducted in the wake of the scandal, without either "483s" or "EIRs." If they are not immediately corrected, FDA takes regulatory actions which can range from the closing of a plant to the withdrawing of a drug to the above-mentioned refusal to approve a new application.

But the heart of your questions seem to focus on whether the FDA process is strict enough to catch these scientific failures. In terms of generics, the answer is "yes." Over 8,000 clones of some 170 brand name drugs have been approved over the last twenty years without a single therapeutic failure. So it would seem that while the scientific process is correct, failures lie elsewhere in the system. These failures did not seem to create health or safety or effectiveness problems which were unique to this crisis. A reading of the FDA recalls over the last five years reveals many examples (in brand and generic companies) of certain batches failing to meet potency, or a mistake mixing in an unwanted ingredient, or a labelling mishap and occasionally a brand name drug being removed from the market.

In summary, when the generic approval process is not corrupted, it works well and from what the FDA has said the generic products which reached the market by bypassing the system seem to have been safe and effective and I have no reason to question their conclusion. If they are not correct, their conclusions will be tested in the courts by consumers who believe otherwise.

Excuse the lengthy answer to this question, but the background is important to understand why and when drugs are withdrawn and when they do and do not pose a safety problem.



American
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The National Professional
Society of Pharmacists

APhA

May 3, 1990

The Honorable Marilyn Lloyd
Chairman, Select Committee on Aging
Subcommittee on Housing and Consumer Interests
717 House Office Building, Annex 1
Washington, D.C. 20515

Dear Chairman Lloyd:

I was pleased to have the opportunity to testify before your Subcommittee on the issue of safety of generic drug products. I am also eager to answer the questions you posed in your March 15th letter. I will restate your question and then provide my response.

1. Are you confident that the FDA procedures to ensure bioequivalency are accurate? Should the current 20% rule be tightened?

It is my opinion that the scientific basis for the FDA awarding a generic drug product an "AB" rating, signifying that it can be considered bioequivalent to the innovator or brand name product, is sound. As long as the FDA investigations and inspections can ensure that the data the FDA scientists review is not fraudulently produced, I am confident in the outcome of that review. The 20% rule is not always applied and is a bare minimum. In cases when the drug being tested has a narrow therapeutic index, the FDA often tightens the requirement before it will approve a drug as AB rated. I agree with a general minimum of 20% and with a case-by-case tightening of that rule as is currently practiced by the FDA reviewers. The need is not for better testing procedures but for more investigation and better oversight of the industry by FDA to prevent fraud.

2. My home state of Tennessee tests generic drugs before allowing them on our Medicaid Formulary. Do you believe state associations or others should also test these generic drugs?

I have mixed feelings regarding the need to have states involved in generic drug approval. While I can understand the need to test those drugs that are not tested by the FDA process, I hate to see a state Medicaid commission spending money on such tests, only to repeat work already performed at the federal level. If the FDA's ANDA process is suspect, it should be fixed, rather than have each state performing a second set of tests at a high cost to the public. There are, however, a number of drugs originally marketed prior to 1938 which are not required to submit bioequivalency data to the FDA. These drugs should be tested by an independent agency to ensure the public of the therapeutic equivalence of those products.

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3. In your testimony, you recommend that consumers consult with their pharmacists to assure themselves that they are receiving the most cost-effective drug product for their condition. Would you clarify the distinction between a professional pharmacist and a pharmacy technician that may serve the public at a retail pharmacy?

Pharmacists are licensed to practice pharmacy. The individual has a Bachelor of Science (BS) degree in Pharmacy (usually 5 years of specialized college education) or a Doctor of Pharmacy (Pharm.D.) (usually 6 years of specialized college education) or both. Pharmacists are trained to not only deliver the drug product to the patient, but also to assure that the prescribed drug -- appropriateness, strength, dosing schedule, dosage form, safety and efficacy in conjunction with other medications -- is the best one for a particular patient.

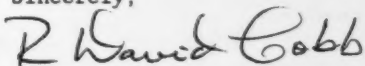
A pharmacy technician works under the supervision of a pharmacist and performs technical tasks the pharmacist deems necessary under the constraints of state law (state pharmacy practice acts). In most states, technicians perform clerical duties such as: answering telephones, handling the cash register, typing labels, and counting tablets or measuring liquids. A pharmacy technician may not provide advice or counsel the patient and may not work without the supervision of a pharmacist.

4. The information that has surfaced regarding the independent laboratories that test the bioequivalency of generic drugs is a concern to me. Are you confident that the labs, which are paid directly by the drug firms, have not been inappropriately influenced by the drug companies?

I am very concerned about those laboratories that accepted an equity interest in the product rather than a simple fee for performing the test. We have recommended that the FDA through regulation, or Congress through legislation, prohibit independent testing laboratories from having an equity interest in the product they are testing or in the company for whom they are testing it. Again, this is an area where increased inspection by the FDA would be helpful to ensure that fraud is not taking place.

I hope that my brief answers to your questions have been of some help in your investigation. If you need any further assistance, please feel free to call upon me or Dr. John A. Gans, executive vice-president of APhA.

Sincerely,



R. David Cobb, Pharm.D.
Immediate Past President
American Pharmaceutical Association

RDC/AHK/mmg

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Charles W. White, M.D.

Reggie A. Henderson, M.D.

April 10, 1990

The Honorable Marilyn Lloyd
Select Committee on Aging
Chairman, Subcommittee on Housing
and Consumer Interests
717 House Office Bldg, Annex 1
Washington, DC 20515

Dear Representative Lloyd:

I hope that my testimony on generic drugs at your hearing on March 1 related to generic drug safety was of some value to your Committee. In answer to the additional questions which were submitted to me - after serving approximately nine years on the Medicaid Formulary Advisory Committee for the State of Tennessee, I believe that Tennessee does have an excellent program for checking and double-checking drugs which have been previously approved by the Food and Drug Administration for marketing to our Medicaid patients. I believe that these same drugs which have been approved for Medicaid distribution can also be used by the public at large to save money on their drug bills.

I believe that there are generic drugs on the market and available for consumers which may not come up to the standard as outlined by the University of Tennessee for our Medicaid patients. Therefore, I do believe that generic drug users in states without such a program are more at risk because some of the companies which market the generic drug may not be checked and double-checked at the state level to be sure that their drugs are, in fact, bioavailable and bio-equivalent.

I believe that as long as the administration of the Medicaid program is left in the hands of the individual states, some method of checking the generic drug should be carried out by each state. I believe that our method in Tennessee is good enough that I would endorse this approach for all states.

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I am interested in patients obtaining the best drug at the most economical price. That goal is obtainable in Tennessee for most older patients if they will have a good communication with their doctor and with their pharmacist. They should certainly do some shopping to see if a cheaper price is available for an individual drug. However, in shopping for this cheaper price in Tennessee, they certainly should check to see if this cheaper price is available on a drug which is also included on the Medicaid Formulary list. If not included on the generic Formulary list, then this drug may not be bioequivalent or bioavailable and may not, in fact, be worth the purchase price. In the issue related to quality vs cost, it is of course imperative that a patient take a drug which does have quality so that the drug is, in fact, used in the proper way in his or her body rather than being excreted unused. Therefore, if there is a question related to quality vs cost, I then try to decide in relation to the disease I am treating the patient for as to whether they deserve a generic drug or a brand name drug which may be of better quality. This must be individualized.

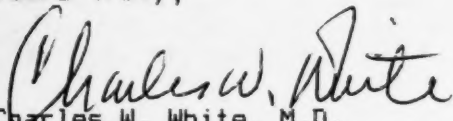
The answer to your third question related to physicians failing to describe the drugs they prescribe and whether or not there is a generic alternative is rather difficult to answer, partly because there is quite a bit of pride on the part of most patients who do not want to admit that they do not have the money to buy the prescribed drug or to ask if there is a generic alternative which might save them some money. It is true that we as physicians due to the press of time may fail to properly communicate with the patient. I am sure that all of us are guilty of this at some time in our daily routine. We should never fail to let the patient know that we care for them as a total person, not just as a patient or a "case". Hopefully, in the future with the changes which are envisioned by the Health Care Financing Administration and by Congress relative to reimbursement of physicians, there will be more physicians available for primary care, and we will, in fact, have more time to spend

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with individual patients. I have no problem whatsoever with physicians providing some factual information to patients related to generic drugs. If a similar plan followed by the State of Tennessee related to approving generic drugs for the Medicaid Formulary were adopted by all of the states, physicians could then provide some information to their patients in a general manner rather than getting down to specifics about each drug or each class of drug. It would be very difficult at the present time to provide patients with any information in writing about each drug or class of drugs which we prescribe. However, it would not be difficult to give them some information about the availability of generic drugs if it could be done in a general fashion.

Again, I hope that my testimony on March 1 and the additional comments in this letter are helpful to your Committee.

Yours truly,

A handwritten signature in cursive script that reads "Charles W. White". The signature is written in dark ink and is positioned above the printed name.

Charles W. White, M.D.

CWW:pf

APPENDIX III



DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of Inspector General

AUG 17 1989

Memorandum

Date *RR Kusserow*
From Richard P. Kusserow
Inspector General

Subject Management Advisory Report: Vulnerabilities in the Food and Drug
Administration's Generic Drug Approval Process (A-15-89-00051)

To James O. Mason, M.D.
Assistant Secretary
for Health

This report discusses material weaknesses in the internal controls of Food and Drug Administration's (FDA) generic drug approval process. Our review was performed at the requests of the Commissioner of Food and Drugs, Dr. Frank Young, and Congressman John D. Dingell, Chairman, House Subcommittee on Oversight and Investigations, Committee on Energy and Commerce. This came as a result of OIG investigation of fraud and corruption within the generic drug approval process which has resulted to date in the convictions of three FDA officials, three generic drug industry representatives and two generic drug firms. The investigation has broadened to identify fraud and misrepresentation in the generic drug approval process, including false statements and claims, as well as product substitution. The Commissioner requested that we identify the weaknesses and vulnerabilities in the system which gave rise to these problems and allowed preferential or detrimental treatment to be given to certain drug manufacturing firms and to recommend corrective action.

We determined that FDA (1) arbitrarily assigns and reassigns drug applications to reviewers based on the reviewers' experience with the drug, (2) lacks adequate guidelines to ensure the consistent review of applications, and (3) needs a quality control system to ensure that applications are properly reviewed and that generic drug firms receive equitable treatment.

These irregularities occurred because there is a material internal control weakness in the generic drug review process that allowed preferential treatment to drug firms. This internal control weakness (1) significantly impairs FDA's mission of assuring a fair generic drug review process, (2) allows employees involved in the process to violate the Department's standards of conduct, (3) could deprive the public of competitively priced drugs, and (4) merits the attention of senior officials. Any one of these four effects fits the criteria for a material internal control weakness included in Office of

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Management and Budget instructions to agencies for implementing provisions of the Federal Managers' Financial Integrity Act of 1982 (FMFIA).

Moreover, FDA has yet to evaluate its generic drug review process as is required by the FMFIA and implementing instructions. The Office of Management and Budget requires Federal agencies to segment their operations into internal control areas, perform risk assessments, and perform internal control reviews of areas with moderate to high risk, and to correct weaknesses identified. Had it conducted the required internal control review of the generic drug approval process, it might have identified and corrected internal control weaknesses that allowed these irregularities to occur.

We discussed our preliminary findings and recommendations with FDA officials on July 10, 1989. FDA is in general agreement and has taken or planned a number of corrective actions.

BACKGROUND

The Drug Price Competition and Patent Term Restoration Act of 1984 (P.L. 98-417, dated September 24, 1984) authorizes FDA to accept abbreviated new drug applications (ANDAs) for generic versions of new brand name drug products first approved by FDA for safety and effectiveness after 1962. Before passage of the Act, ANDAs were permitted for generic versions of only drug products first approved between 1938 and 1962. Generic drugs, to be approved for marketing by FDA, must be therapeutically equivalent to brand name drugs already approved by FDA as safe and effective. Under the Act, a manufacturer must show that its product is bioequivalent--that the active ingredient is absorbed into the human body at about the same rate and extent as that of the innovator or brand name product.

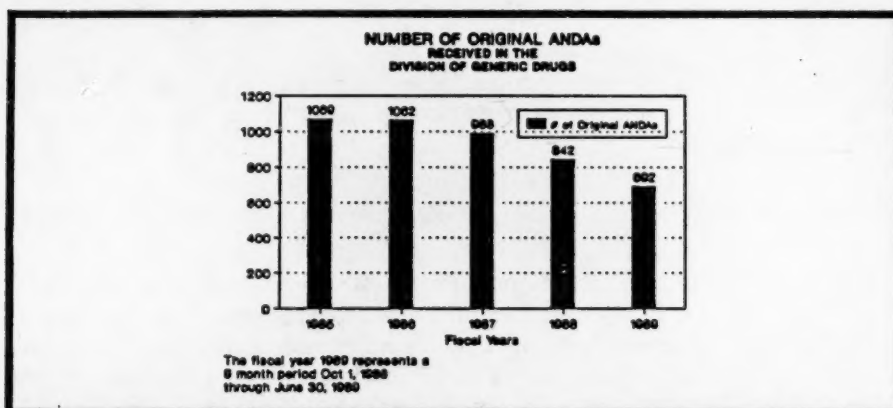
An ANDA contains information on the drug product's bioequivalency, chemistry, labeling, manufacture, and controls. Data to support the drug's safety and effectiveness have already been provided to FDA by the manufacturer of the brand name drug. Therefore, generic drug manufacturers do not have to submit safety and effectiveness data in their abbreviated applications because their product should be a duplicate of or similar to the brand name product.

FDA's Division of Generic Drugs, located in the Center for Drug Evaluation and Research, reviews and evaluates ANDAs, their amendments and supplements, and determines approvability based on medical and scientific data findings. It is com-

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prised of a review support branch, a labeling review branch, and three ANDA review branches. The Division of Generic Drugs has a budget of about \$15 million. In early 1985, the Division of Generic Drugs recruited 22 new employees, increasing the staff from 32 to 54. Since then the staff has remained at that approximate level.

According to FDA officials, in late 1984 there were a large number of applications which caused a substantial backlog and created an extremely stressful climate in FDA. The workload since 1985 has been steadily decreasing as shown in the chart below:



There is a perception within the industry that the firm to receive first approval will have a long-term, competitive advantage in terms of market share and revenue over later entrants into the marketplace. According to FDA, companies are anxious to receive first approval to market a new generic product so they can enjoy a period during which they are the exclusive marketer of the product.

The Director of FDA's Division of Generic Drugs, in a presentation before an FDA and Industry Workshop in East Hanover, New Jersey on October 1, 1987, commented on carrying out the provisions of the Act as follows:

"Our most serious problem, in my opinion, was the seemingly almost unrelenting pressures applied by a handful of firms, all of which would like their applications to be reviewed first and approved yesterday. Being pressured repeatedly and at times from all sides it seems, gets old, is very fatiguing, and counterproductive. We cannot give one firm

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preferential treatment without being unfair to another and we are not willing to favor one at the expense of the other."

In June 1988, the Subcommittee on Oversight and Investigations of the House Committee on Energy and Commerce received allegations of improprieties associated with the generic drug approval process at FDA. Specifically, it was alleged that certain employees in FDA's Division of Generic Drugs' ANDA review branches willfully manipulated the application review process to give preferential treatment to certain pharmaceutical companies.

The Subcommittee referred criminal allegations to the Office of Inspector General for investigation. The OIG initiated an investigation into these allegations under the auspices of the U. S. Attorney's Office. Subsequently, criminal charges were lodged. To date, three FDA employees, three drug company employees, and two companies have pleaded guilty to charges of corruption. This investigation is continuing.

As serious questions arose with respect to procedural and ethical deficiencies in the generic drug program, FDA initiated an internal assessment of the ANDA approval process and its conflict-of-interest procedures. According to FDA, to avoid interference with the ongoing criminal investigation at that time, FDA's review was a limited one which did not include interviews with the generic drug review staff. A report was issued by FDA in December 1988, recommending limiting access by generic drug industry representatives to FDA employees reviewing their applications and intensifying conflict-of-interest training.

FDA began implementing these recommendations in January 1989. Generic drug industry representatives are no longer allowed to make unannounced visits to the offices of FDA reviewers to discuss their applications. Meetings must be requested by industry representatives in advance with an agreed upon agenda, held away from the reviewers' work space, and held in the presence of FDA supervisory personnel. In addition, reviewers are not required to answer application status calls from drug firms.

We note that FDA's Fiscal Year 1990 budget request, transmitted to the Congress on April 3, 1989, included \$100 million in user fees, of which \$15 million was for the generic drug approval process. These user fees would enable FDA to charge the full cost of reviewing ANDAs, with the revenue coming to FDA to support these activities. The fee for generic drug applications would be about \$18,000 per application.

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SCOPE AND METHODOLOGY OF REVIEW

The purpose of our review was to identify vulnerabilities in the generic drug application review process that could allow preferential or detrimental treatment to be provided to certain drug firms. It did not include an evaluation of the scientific merits of the proposed generic drugs, nor did it attempt to evaluate the appropriateness of FDA's approval or disapproval of the generic drug applications.

We reviewed statutes, regulations, policies, procedures, and guidelines relating to the review and approval of generic drug applications. Extensive interviews were held with FDA management and supervisory personnel and reviewing chemists. Applications were reviewed to familiarize ourselves with information that must be submitted by companies for generic drug approval. Workload data from October 1, 1988 to June 30, 1989 was obtained and analyzed, as well as reports generated by the ANDA management information system.

Our review was performed primarily in FDA's Division of Generic Drugs within the Center for Drug Evaluation and Research. Our work was done between May 15, 1989 and July 7, 1989 at FDA headquarters in Rockville, Maryland.

ASSIGNMENT OF ANDAs

Presently, ANDAs are assigned to one of three chemistry review branches by a consumer safety officer. The assignment to a particular branch is usually based on a branch's experience with previously submitted applications for similar drug products. The branch chief then assigns the ANDA to a specific chemist for review based on the chemist's experience with the drug. Weaknesses in the internal control structure of this assignment process allowed preferential treatment to drug firms.

Favoritism was provided to certain generic drug firms, notwithstanding Federal Regulation (45 CFR 73) which prohibits Federal employees from giving preferential treatment to any person. Preferential treatment was provided by (1) assigning ANDAs to a fast reviewer over a slow reviewer and (2) reassigning applications to lengthen the review period. In addition, we noted that preferential treatment may be provided by assigning competing firms' ANDAs for the same drug to the same reviewer.

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Some chemists review ANDAs more quickly and, consequently, are assigned a larger workload as shown in the table below:

Action Letters ^{1/} by Chemists
October 1, 1988 to May 31, 1989

Review Chemists	Not Approvable Letters	Approval Letters	Total	Applications Pending
A	209	17	226	73
B	18	3	21	25
C	137	20	157	54
D	67	5	72	34
E	16	0	16	25
F	115	14	129	71

As shown in the table above, during the 8-month period from October 1, 1988 to May 31, 1989, one chemist reviewed and prepared action letters for 226 applications, while another chemist prepared 21 action letters. A branch chief could favor a particular company by consistently assigning the company's ANDAs to fast reviewers while penalizing other companies by consistently assigning their ANDAs to slow reviewers. A former branch chief in the Division of Generic Drugs admitted doing this. We noted that the Division Director was not aware of this productivity variance and was not routinely monitoring this activity.

A drug firm official disclosed, in testimony on May 11, 1989 before the Subcommittee on Oversight and Investigations of the House Committee on Energy and Commerce, that a former branch chief delayed an application for its company by reassigning it to three different chemists even though it was nearly ready for chemistry approval by the initial reviewing chemist. A chemist told us the same branch chief expedited applications by reassigning them from certain chemists to others who could complete the review in a shorter period of time.

^{1/} Action letters are approval or not approvable letters issued to drug firms by FDA upon completion of the review of the firms' generic drug applications.

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We also identified a potential area of vulnerability caused by the lack of controls over branch operations. This could occur when a branch chief assigns applications for the same drug product from competing companies to the same chemist for review. Consequently, a chemist could deliberately identify fewer deficiencies in one application while identifying numerous deficiencies in a competitor's application. Because both companies must correct all deficiencies in their amended applications to FDA, the company with the fewest deficiencies can respond more quickly. This company's application could then receive approval ahead of its competitor's application.

While we did not prove or disprove that favoritism had occurred from this vulnerability, we noted three instances where the same drug product from competing companies was assigned to the same chemist for review. In the first instance, applications for the drug Sulindac submitted by four different companies and received in FDA on March 3, 1989; March 14, 1989; April 21, 1989; and April 24, 1989, were assigned to the same chemist for review. In the second instance, applications for the drug Timolol Maleate submitted by three different companies and received in FDA on October 24, 1988; October 24, 1988; and October 28, 1988, were assigned to one chemist. In the third instance, applications for the drug Amoxapine submitted by three companies and received in FDA on June 7, 1988; June 9, 1988; and June 24, 1988, were assigned to the same chemist for review.

APPLICATION REVIEW PROCEDURES

The FDA has established few standard operating procedures for chemists to use and, therefore, cannot assure that ANDAs will be reviewed in a comprehensive and consistent manner. The lack of procedures may indirectly favor one company's application for which a chemist may do a minimal review and adversely affect another company's application for which a chemist may do an exhaustive review. It could also affect when the applications are actually reviewed.

One chemist told us that chemists generally reviewed applications differently based on their education, training, and experience. This chemist stated that if three chemists reviewed the same application, each review would probably be different. A second chemist, who took over another's work, told us about deficiencies which were not included in those reviews. This chemist said that if other chemists looked at these reviews, they also might have found deficiencies which might have been overlooked. This chemist stated that guidelines are needed so that a chemist in one branch will conduct a review similar to a chemist in another branch.

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The ANDA reviews are generally conducted on a "first-in, first-reviewed" basis. This policy applies to both original ANDAs and amended ANDAs. Exceptions to the "first-in, first-reviewed" policy were discussed in a May 10, 1989 memorandum from the Director, Division of Generic Drugs, to Division staff. The Director said an application could be reviewed out of sequence only when labeling issues or minor chemistry deficiencies existed. Because such items can be reviewed in a short period of time, it is not necessary to delay approval by placing the application at the bottom of the review line. Therefore, amended applications for these minor deficiencies can be reviewed and approved before other amended applications with major deficiencies that were sent to FDA earlier. If this policy is not uniformly applied and actions not properly documented, drug companies may complain that FDA is penalizing them while giving preferential treatment to other firms. We noted FDA has no system in place to assure proper implementation of this policy.

QUALITY CONTROL SYSTEM

FDA lacks a quality control system that assures the fundamental integrity and fairness of the ANDA review process. A well designed and properly implemented quality control system should provide all levels of management with the assurance that they are doing their job properly, timely, consistently, fairly, legally, and efficiently. A good quality control system should also provide management feed-back when policies and procedures are not being followed, need revision, or need to be established. At a minimum, FDA should establish a system that incorporates the controls we are recommending.

BIOEQUIVALENCY TESTING

Drug firms are not required to submit bioequivalency drug samples to the FDA with their ANDA applications. FDA recently learned of a case where a drug firm substituted the ingredients of a brand name product as its own. FDA is unaware of the extent to which other substitutions may be occurring. We noted FDA has some action underway or planned to assess whether generic drugs presently being marketed are consistent with the chemicals included in the bioequivalency tests. According to FDA, samples from a large variety of generic drugs were recently obtained from a laboratory that performs premarket testing for drug firms. FDA is analyzing these samples to determine whether firms have submitted valid samples with their applications.

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FDA is proposing to amend its current bioequivalency regulations to require the retention, for a specified period, of samples of the test product and reference standards used in performing bioequivalent testing of drug products, and when specifically requested, to provide the samples to FDA. A draft version of this proposed rule is being circulated within FDA for comment.

USER FEES

The generic drug approval process depended in large measure on the "honor system." OIG investigations to date have demonstrated that this can no longer be relied upon. Increased surveillance and independent testing is necessary. The add on costs should be borne by the industry in the form of user fees and not at taxpayers' expense. This is consistent with a President's Council on Integrity and Efficiency report on user fees, issued on February 10, 1989, which stated that FDA has not taken full advantage of user charges as a means to offset the costs of providing services and special benefits to identifiable recipients. We continue to support the concept of user fees for generic drug applications. Such fees would enable FDA to obtain the resources needed to improve the operation, management, and oversight of its generic drug program.

CONCLUSIONS

Our review showed that FDA does not have adequate internal controls over the ANDA review process to maintain its integrity. This lack of controls made the ANDA review process susceptible to manipulation and preferential treatment.

However, the conditions under which applications are now reviewed within FDA are different. Generic drug industry representatives are no longer allowed to make unannounced visits to the office of FDA reviewers to discuss their applications. According to FDA access by generic drug industry representatives to FDA employees reviewing their applications has been controlled and conflict-of-interest training intensified. In addition, reviewers are not required to answer application status calls from drug firms. These actions limit the industry's access to and personal contact with FDA reviewers and were brought about as a result of FDA's internal assessment review. These are steps in the right direction.

These actions, however, do not address the weaknesses that allowed FDA employees to manipulate the process. The current arbitrary system for assigning ANDAs to reviewing chemists could permit favoritism to certain drug firms. A system that

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would allow assignments of applications on a random or similar basis, in our view, would help prevent this potential type of favoritism. The FDA accepts that it has fast and slow reviewers. We believe, however, that reviewers' speed could be made more equal if all reviewers worked from uniform review standards. Consequently, uniform review procedures and operating guidelines for assigning, reassigning, reviewing, and tracking under the ANDA process are necessary to avoid the appearance or reality of FDA employees favoring certain drug firms.

The ANDA reviews are generally conducted on a "first-in, first-reviewed" basis. We believe this is a good policy and, if properly implemented, will serve to bring generic drugs to market in a timely manner. However, if this policy is not uniformly applied or actions not properly documented, drug companies may complain that FDA is giving preferential treatment to one firm over another.

Had FDA evaluated the generic drug review process under the provisions of the FMFIA, it may have identified and resolved the material internal control weakness in the generic drug application review process. Now that the weakness has been identified, we believe it should be disclosed in reports required by the FMFIA as a material weakness and corrective action monitored through the FMFIA tracking system until the weakness is resolved.

RECOMMENDATIONS

We recommend that you direct FDA to improve internal controls over the generic drug review process by:

- requiring branch chiefs to monitor and report to the division director on the progress of ANDA reviews;
- developing policies and procedures for the random assignment of ANDAs to reviewing chemists, or for other appropriate methods for reducing the opportunity to show any partiality to applicants;
- requiring each request for ANDA reassignment to another chemist, after the initial assignment, be approved and justification included in the ANDA file;

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--supplementing the May 10, 1989 memorandum regarding exceptions to the "first-in, first-reviewed" policy by defining and providing examples of minor chemistry deficiencies and including the supplement in the division's standard operating procedures manual;

--ensuring that exceptions to the "first-in, first-reviewed" policy are uniformly applied by all chemists;

--ensuring that reasons for reviewing and approving an ANDA out of sequence from the order it was received are properly documented in the ANDA file;

--developing policies and procedures for use by supervisory and review chemists to ensure the consistent, comprehensive review of applications;

--requiring drug firms to submit bioequivalency samples with the ANDA and validating the authenticity of the samples submitted;

--establishing a quality control review system which includes uniform standards for the review of generic drug applications and operating guidelines for the generic drug application review process; and

--disclosing in reports required by the FMFIA that there is a material weakness in the internal control structure for the generic drug approval process that allowed preferential treatment to drug firms, and monitoring corrective action until the weakness is resolved.

If you or your staff wish to discuss these issues further, please let me know or contact Daniel W. Blades, Deputy Assistant Inspector General for Audit. We would appreciate receiving a status report within 14 days on the action taken or contemplated on our recommendations. A copy of this report is being sent to other interested departmental officials.

EDITORIALS

Generic drug products

Recent widely publicized illegal and unethical activities by a few generic drug companies and FDA employees have called into question the quality of multisource prescription drug products. This issue is of direct and immediate concern to pharmacists, the health professionals responsible for selecting the source of drug products dispensed to patients. The matter is especially acute for pharmacists involved in bid purchasing of pharmaceuticals.

Briefly, what happened is that some generic drug companies made illegal gifts to three officials in the FDA generics division. Those employees have now resigned. Separately, it was shown that data were falsified in the applications for approval of certain generic drug products.

Many of the improprieties in the generic-approval process were brought to light by Congressman John D. Dingell (D-Mich.), who has a long history of interest in drug legislative and regulatory issues. The FDA, to its credit, has responded to the crisis promptly and forcefully. Its actions include the following:

- Withdrawing the marketing approval of 30 generic products made by four manufacturers because of uncertainties about the data submitted by the firms.
- Sampling and analyzing the 30 most-prescribed generic drug products, representing approximately 75% of the generic market. The samples will be tested for potency, dissolution, composition, and other specifications.
- Analyzing product samples that had been submitted by generic firms before marketing, to determine whether the companies submitted valid samples.
- Inspecting the production facilities of 31 manufacturers of generic drug products. Some of these inspections involve the plants of brand-name manufacturers that also make generic products.
- Inspecting contract laboratories that do premarket testing of generic products, to affirm that product approvals are based on valid data.
- Implementing internal organizational changes, including added staff and new quality control oversight, that will strengthen generic-product review procedures.

In addition, the Department of Health and Human Services is seeking new legislation that will clarify, strengthen, and broaden FDA's authority to act promptly against irregularities in conjunction with applications for product approval.

These measures merit the strong support of pharmacists, other health professionals, and the general public. One hopes that the deplorable, headline-attracting lapses in the approval process for generics have been rare and isolated incidents. Generic products are dispensed for one third of all prescriptions, and the experience of physicians, pharmacists, and patients suggests

that these products continue to be safe and effective. Nevertheless, this question is too important to be answered by anything less than objective, scientific evidence. The findings of FDA's analyses and inspections should yield that evidence and serve as a guidepost for any further actions that may be necessary.

It is well to recall that the generic drug industry received a substantial boost five years ago when federal drug laws were amended.¹ Previously, in order to market a generic version of a product that had been approved after 1962, the manufacturer had to prove the *safety and efficacy* of the generic product. Following enactment of the 1984 amendment, only *bioequivalency* has had to be documented. This easing of the approval process led to dramatic growth in the number of generic-product applications submitted to FDA. When FDA reviews these abbreviated new drug applications, it evaluates reports of data submitted by the manufacturer; it does not perform independent bioequivalency testing of the products. The HHS Inspector General recently recommended that generic manufacturers be required to submit bioequivalency samples with their applications and that FDA validate the authenticity of the samples submitted. It may be desirable to overhaul FDA procedures in this manner to further restore public confidence in the nation's medication supply.

A belief that has prevailed among hospital pharmacists for decades is that all generic versions of a product are not necessarily equal. This belief is reflected in the drug-product procurement procedures of hospitals and group purchasing organizations, which consider numerous factors in addition to cost in their selection of multisource products. Many pharmacists in organized health-care settings are guided in this respect by an ASHP practice standard.² Among the factors that this document says pharmacists should review in evaluating prospective suppliers are the following:

- Analytical control, sterility testing, and bioavailability data, and descriptions of testing procedures for raw materials and finished products;
- Product recall history;
- Compliance with official compendial standards;
- The identity of the fabricator of the final dosage form; and
- The availability of therapeutic, biopharmaceutical, and toxicologic information.

Selecting multisource drug products is one of the most important responsibilities of pharmacists. It is a task that calls into play their unique knowledge and professional judgment. In light of the current controversy, pharmacists should redouble their efforts to carry out this responsibility with the utmost of care and integrity.

1. Hogan GF. Repercussions of the Drug Price Competition and Patent Term Restoration Act of 1984. *Am J Hosp Pharm.* 1985; 42:849-51.

2. ASHP guidelines for selecting pharmaceutical manufacturers and distributors. *Am J Hosp Pharm.* 1984; 41:331-2.

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